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Southern Medical Association, Thirty-Second Annual Meeting, Oklahoma City, November 15-18

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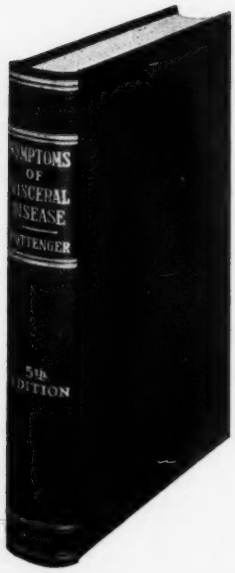

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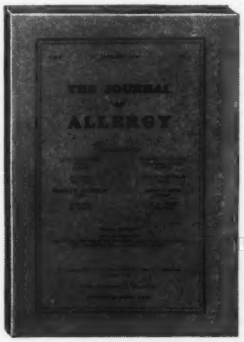

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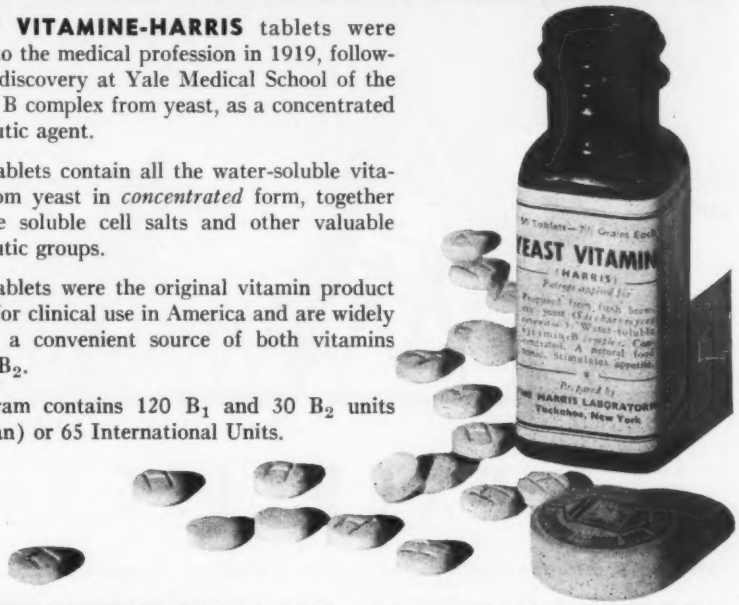

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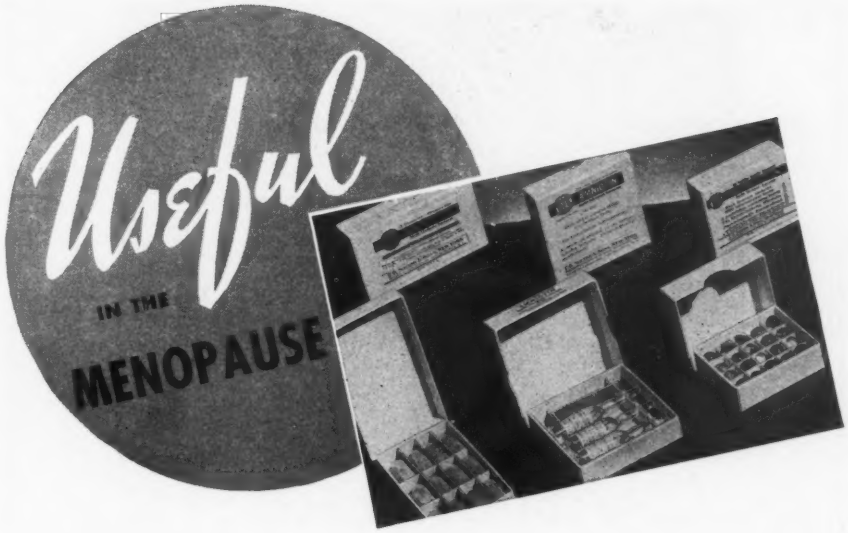

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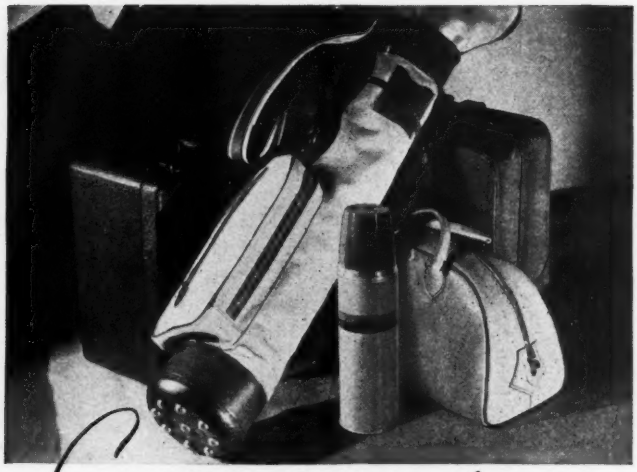

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*Bunch, Geo. H., Southern Medicine & Surgery; July, 1937.

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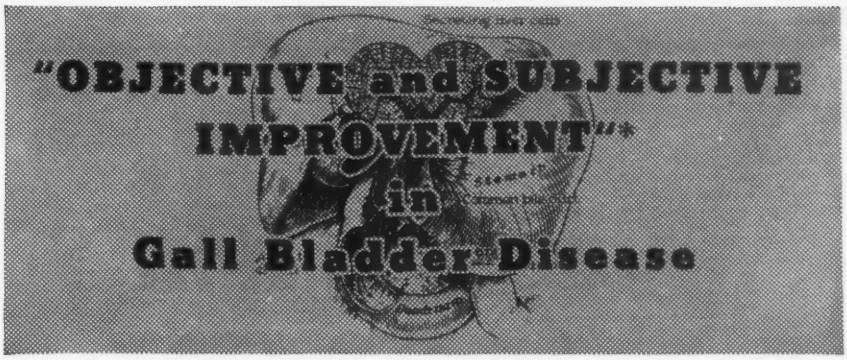

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*Brown, C. F. G. and Dolkart, R. E., J.A.M.A., 108:458 (February 6) 1937.

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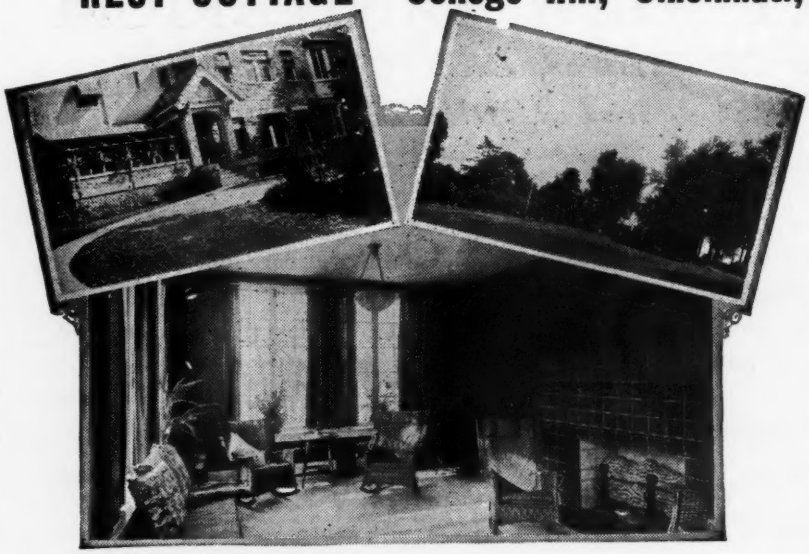

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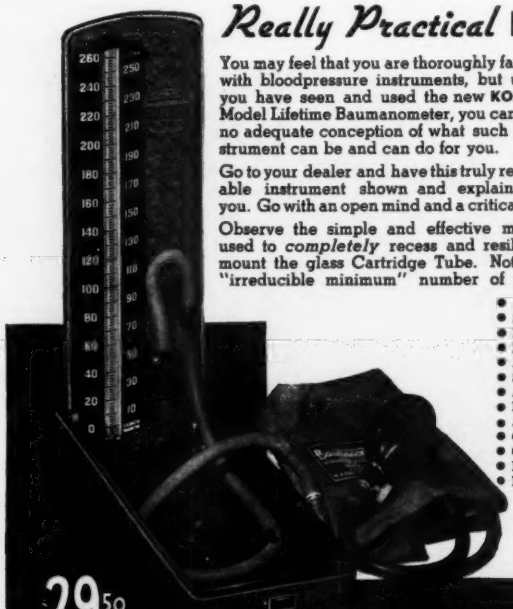

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JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 31 JUNE 1938 Number 6

PSEUDOMYCOSIS: INDOLENT LEG ULCER*

A STUDY OF 54 PATIENTS

By J. F. HAMILTON, M.D.
Memphis, Tennessee

In December, 1927, the author encountered two patients who presented strikingly peculiar ulcers. Material from these ulcers was examined both in direct smear and by culture; micro-organisms were found which were believed to be different from any previously described. Since he was unable to define or classify this micro-organism and believed it to be the etiologic agent responsible for the chronic ulceration, notes were made of the lesion and its characteristic micro-organism.[1 2] To our delight in December, 1928, Castellani[3] published a report on a lesion of a similar character and gave the disease the name, "pseudomycosis." The micro-organism was called *Micrococcus myceticus*. The similarity of his description of both the ulcer and the etiologic agent coincided so closely with the disease which we had observed, that we concluded the two were synonymous.

Meleney,[4 5] Kilbourne[6] and others[7 8 9] have subsequently described "chronic undermining ulcer" and "lacunar ulcer." From the clinical behavior, bacteriologic characteristics and appearance of the photographs of these ulcers, one wonders whether these lesions have a common etiologic background. However, as the bacteriologic data in these papers were incomplete, it is impossible to be certain of this fact.

A preliminary report on pseudomycosis was published by the author in November, 1930. Since that time a total of 54 patients have been studied, sufficient data having been accumulated to present a complete and critical analysis of 44 of these.

This affection seems to have no particular geographical distribution. Castellani first recognized it in Ceylon 27 years ago. Patients who reside in urban and rural communities seem to be affected alike. The social status of the patient with his hygienic surroundings does not vary the incidence of the disease. Thirty-one of the 44 patients were under 31 years of age (*Table 1*).

Table 1

NUMBER OF PATIENTS IN EACH AGE GROUP

Age Group	No. of Patients
1 through 10	1
11 through 20	17
21 through 30	13
31 through 40	4
41 through 50	6
51 through 60	2
61 through 70	1

The history of onset as related by most of the patients is insidious. They frequently indicated "a mosquito bite, spider bite or a briar scratch" as the cause of the ulcer. A stinging or burning sensation and pruritus develop followed by swelling, redness and, less frequently, fever. Twenty-four to 48 hours later, if the infection begins in the superficial layers of the skin, a small pustule forms in the center of the inflammatory area. Usually the small pustule has been opened by the patient or his family physician, leaving an ulcer. Instead of healing as an ordinary pustule, the small ulcer continues to grow larger despite therapy.

On the other hand, if the infection begins in the deeper structures or becomes disseminated from the original focus, the signs of inflammation will be more pronounced; most likely as a hard, brawny cellulitis. Constitutional symptoms of greater or lesser degree usually are associated with this cellulitis; surgical incision of such areas only makes bad matters worse.

Upon first glance the ulcers impress one as being extraordinary. Most of them have a my-

*Read in Section on Pathology, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

*From the Dr. Willis C. Campbell Clinic.

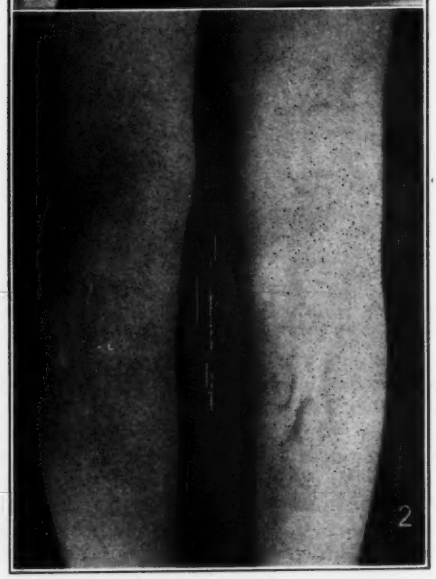

Fig. 1. Miss A. G. (No. 05684), aged 11. Photograph on admission, June 12, 1929, shows right angle contracture at the knee and multiple mycotic-like ulcers in the popliteal space, right leg. The duration was nine months. September, 1928, the first ulcer appeared near the right external malleolus. December 1, the popliteal space became swollen and painful, and was incised just before Christmas. A bloody fluid was obtained. There was no improvement, and February, 1929, the upper third of the tibia and popliteal space were explored; no osteomyelitis was found. The wound failed to heal.

Fig. 2. Miss A. G. (No. 05684), aged 12. Photograph, August 30, 1930, shows the ulcers healed and contracture corrected. Duration of the treatment was fourteen and a half months; duration of the disease, twenty-three and a half months.

cotic appearance which probably prompted Castellani to give this clinical entity the name, pseudomycosis. The slowly spreading type shows round, punched-out, fairly deep lesions with slightly rolled edges and a necrotic, myxomatous base. The rapidly spreading type has thin, irregular, undermining edges and a myxomatous or pale granulation tissue base. These ulcers vary in size from a few millimeters to 10 centimeters in diameter. The lesion is limited entirely to the skin and subcutaneous tissues unless the surgeon's scalpel has opened the way to the deeper structures.

Most of the patients on first examination had multiple ulcers on one lower extremity which were of a few days' to several years' duration, the average being 2½ months. Two patients had ulcers on both lower extremities; one was considered as an auto-inoculation from the primary ulcer. In this series of patients only one ulcer was situated above the knee (*Table 2*).

Table 2

LOCATIONS OF ULCERS, NUMBER OF PATIENTS, AS WELL AS LIMBS INVOLVED

Location of Ulcer	No. Patients	Limb	
		R	L
Patella	1	0	1
Popliteal	5	3	2
Upper third leg	1	1	0
Middle third leg	15	10	5
Lower third leg	5	3	2
Ankle	5	1	4
Foot:			
Dorsum	5	3	2
Plantar	1	0	1
Multiple	6	2	4

In five patients some impairment of the circulation was noted. One had arterial and venous impairment, one arterial, one venous impairment, and in two the ulcers formed in a cicatrix from an old osteomyelitis. These findings were considered as coincidental and of secondary importance.

The leukocytic response to the infection is mild except in the active, undermining stage of the disease. Eighteen thousand five hundred leukocytes per cubic mm. with 82 per cent polymorphonuclear-neutrophils have been encountered in the presence of a cellulitis with abscess formation. Anemia attributable to the infection has not been observed. Wassermann and Kahn reactions were negative in all the patients.

A carefully taken history, a painstaking physical examination and intelligent laboratory investigation are essential prerequisites to the diag-

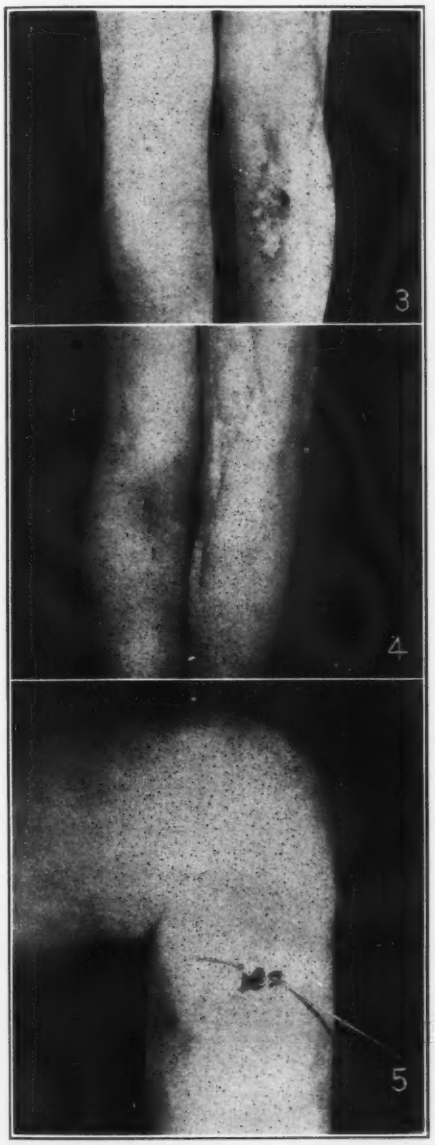

Fig. 3. Miss A. G. (No. 05684), aged 14. Photograph, August 11, 1932, shows recurrent ulcer in the two-year-old healed scar of one month's duration. Four weeks ago the ulcer appeared spontaneously in the old healed scar. Home remedies failed to promote healing.

Fig. 4. Miss A. G. (No. 05684). Photograph, August 11, 1932, with legs crossed to show the manner of auto-inoculation. About time of admission to hospital, August 8, auto-inoculated ulcer appeared in left leg, which, when legs are crossed, coincides exactly with recurrent ulcer in old scar.

Fig. 5. Miss A. G. (No. 05684). Photograph, August 11, 1932, shows the undermined, auto-inoculated ulcer on left leg.

nosis of pseudomycosis. The physician should never make a diagnosis of pseudomycosis just by looking at the ulcer coupled with the facts in the history. Neither should he content himself by making swabs and sending them to the laboratory with the inadequate request, "Culture material on swabs from ulcer." Otherwise the laboratory will probably report the culture as positive for hemolytic streptococcus, and thus the full significance of the condition is not realized until after a long period of therapy with negative results. At least the presumptive clinical

Fig. 6. Miss A. G. (No. 05684). Photograph, September 21, 1932, shows the ulcer of the right leg healed. The ulcer of the left leg healed November 7, 1932. Duration of treatment was ten weeks and twelve weeks, respectively. Duration of the disease was four months.

Fig. 7. Miss M. P. (No. 33818), aged 13. Photograph, May 30, 1934, shows mycotic-like ulcer 2 inches x 1 inch with undermined edges just below the head of the left fibula. Duration was two and a half months. Discolored skin at the upper border was incised June 2, 1934. The patient was treated by a dermatologist for 2½ months. Various medicaments, alpine lamp and adhesive strapping had been applied with no improvement.

diagnosis should accompany the original laboratory request.

In differentiating this lesion from other affections one must consider the true mycoses, syphilis, tuberculosis, varicose ulcers and tularemia. The author particularly wishes to stress the laboratory aspects of this disease to prevent erroneous reports that may come from an uninformed laboratory personnel. Until the laboratory characteristics of this disease are thoroughly understood we shall continue to get reports as follows: "Culture reveals gram-positive cocci in chains, streptococcus or hemolytic streptococcus." If hemolytic streptococci are reported from an ulcer one should immediately become suspicious that the condition may be pseudomycosis.

Morphology and Staining Reactions.—The micro-organism is non-motile and no spores have been demonstrated. Direct smears made from open ulcers and unopened lesions showed gram-negative cocci in 19, gram-negative and positive

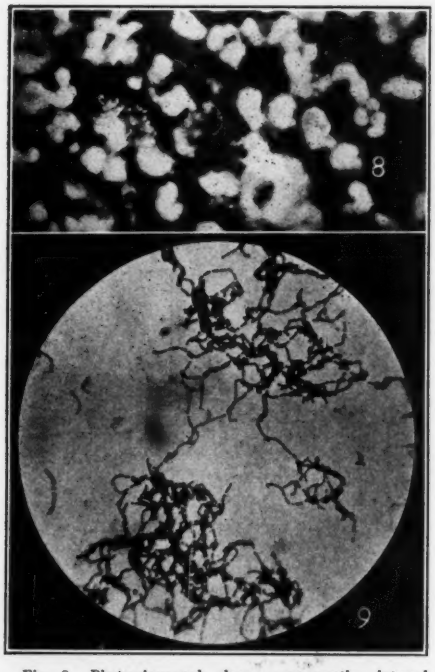

Fig. 8. Photomicrograph shows gram-negative intracellular and extracellular diplococci and gram-negative cocci in short chains in direct smear from the ulcer of Miss M. P. (No. 33818).

Fig. 9. Photomicrograph shows M. myceticus from dextrose brain broth culture from the ulcer of Miss M. P. (No. 33818).

Fig. 10. Miss M. P. (No. 33818). Photograph in July, 1934, shows extension of the ulcer at the upper posterior border and healing at the distal portion.

Fig. 11. Miss M. P. (No. 33818). Photograph, September 3, 1934, shows enlarging daughter ulcer in popliteal space which formed following incising of the undermined skin August 11. On June 2, 1934, a flap of skin overlying a sinus was incised radially. There was no reaction. On August 11, 1934, the procedure was repeated. Severe systemic reaction occurred with temperature 103° and extensive cellulitis of the popliteal space and upper third of the calf of the leg. After 72 hours the reaction subsided following spontaneous rupture of an abscess in the popliteal space. The daughter ulcer appeared a few days later.

Fig. 12. Miss M. P. (No. 33818). Photograph, January 8, 1935, shows a narrow strip of healthy looking skin, the remains of a wide strip of skin which separated the ulcers as shown in Fig. 11.

cocci in 11, gram-positive cocci in 10, and negative smears in 4. Smears made from open ulcers frequently revealed mixed flora, cocci of different kinds and bacilli. Smears made from previously unopened lesions showed cocci only. The number, size, shape and staining qualities of these "intracellular" micro-organisms make it extremely difficult, in many instances, to differentiate them from the gonococcus. But the frequent presence of short chains in these smears will help one to avoid this error.

Stained smears made from direct culture and subcultures on artificial liquid media have always revealed predominantly gram-positive cocci in chain formation.

Castellani again has called attention to another micro-organism which he named *"Micrococcus metamyceticus."* He states that among other things it differs from the *"Micrococcus myceticus"* in that it is constantly gram-negative and occasionally tends to grow as a coccobacillus. This micro-organism has not been encountered in this study. No bacteria resembling fungi or yeast cells have been recovered from these ulcers.

Cultural Characteristics.—The *Micrococcus myceticus* is fastidious in its growth habits and special media are required to recover it consistently in direct culture, though it can be encouraged to grow on ordinary media following subculturing on favorable media. Uniformly good success has been obtained in recovering the micro-

Fig. 13. Miss M. P. (No. 33818), aged 14. Photograph March 15, 1935, shows the ulcer at its largest size, four inches in its greatest diameter. Note several pinch grafts applied March 13, 1935.

Fig. 14. Miss M. P. (No. 33818). Photograph, June 22, 1935, shows the ulcer healed. The duration of our treatment was thirteen months; duration of the disease, fifteen and a half months.

Fig. 15. Dr. A. S. B. (No. 26102), aged 49. Photograph, August 29, 1930, shows absence of the right fifth metatarsal and fifth toe removed three weeks previously with infected wound and a recently formed ulcer near the lateral malleolus. In February, 1929, roentgen ray therapy was directed to the bunionette distal head of the fifth metatarsal bone. Three months later the soft tissue sloughed, leaving a sinus. August 6, 1930, the fifth toe and fifth metatarsal were removed for osteomyelitis of the latter. Seven days postoperatively an inflammatory reaction of the right foot occurred with pain beneath the external malleolus. It was incised twice beneath lateral malleolus. Bloody fluid was obtained at the first operation; white flecked, serous fluid at the second. Amputation was advised for osteomyelitis of the tarsal bones. On admission only marked osteoporosis was evident.

Fig. 16. Dr. A. S. B. (No. 26102). Photograph, October 6, 1930, shows ulcer in wound almost healed. Duration of treatment was five and a half weeks; duration of the disease, over two years.

Fig. 17. Mr. C. L. (No. 28945), aged 17. Photograph, December 15, 1931, shows an irregular ulcer with undermined edges middle third over left shin. The duration was three months. The patient stated that the ulcer followed "chigre bite." In the previous month the ulcerous area had been incised three times. Extensive cellulitis occurred adjacent to the ulcer.

Fig. 18. Mr. C. L. (No. 28945). Photograph, January 8, 1932, shows the undermined flap of skin, a characteristic feature of the disease, three weeks after admission or sixteen days after the overlying skin had been incised.

organism in direct culture on blood agar, dextrose brain broth, and Loeffler's blood serum. Pure cultures, 12 in all, in dextrose brain broth and on blood plates have been obtained from previously unopened lesions and from some of the open ulcers following the use of strong antiseptic solutions which had previously destroyed the secondary invaders. Thirty-two of the primary cultures had a mixed growth in them.

On streaked blood agar plate, in twenty-four hours the colonies were pin-point, elevated, grayish-white, round, smooth, glistening, not confluent and invariably hemolytic. The zone of hemolysis is frequently 5 mm. wide in 18 to 24 hours. Poured and streaked blood agar plate colonies showed much larger zones of hemolysis cultured anaerobically at room temperature than did the ordinary hemolytic streptococcus under the same conditions. At incubator temperature this difference was not marked.

On dextrose brain broth, growth was abundant, in long chains which became entangled, formed large flocculi and settled out of solution. A series of original, pure cultures lived in the original tubes of media from two to fifteen and a half months; average six and six-tenths months. Occasionally, new cultures may die when only a few days old.

On Loeffler's serum, growth was fluent, colonies elevated, round, smooth, grayish-white, and glistening. No liquefaction occurred. The organism lived well on this medium.

Any growth was unusual upon direct inoculation into nutrient broth, but eventually, though not consistently, the cocci could be trained to grow.

Fig. 19. Mr. C. L. (No. 28945). Photograph, April 5, 1932, shows the healed ulcer. Duration of the treatment was three and a half months; duration of the disease, six and a half months.

Due to our inability to grow the micro-organism consistently on nutrient broth, it was found necessary in studying the action of *Micrococcus myceticus* in various sugars to add the sugars to brain infusion broth or some other enriched medium. The results of these studies are recorded in *Table 3*.

Table 3

REACTION OF MICROCOCCUS MYCETICUS IN SUGAR MEDIA

Sugar	M. Myceticus
Dextrose	0 or A
Laevulose	A
Maltose	A
Galactose	0 or A
Saccharose	0 or A
Lactose	A
Mannite	0
Inulin	0
Dulcitol	0
Isotal	0
Inositol	0
Adonitol	0
Arabinose	0
Amygdalin	0
Salicin	0 or A
Sorbitol	0
Raffinose	A

0 = No acid, A = Acid.

Pathogenicity.—The micro-organism is a definite pathogen. In many patients it produces

Fig. 20. Miss M. T. (No. 34661), aged 27. Photograph, October 6, 1934, lower third left leg, shows multiple ulcers with excoriation of the surrounding skin. The duration was eight weeks.

Fig. 21. Miss M. T. (No. 34661). Photograph January 25, 1935, shows healed ulcers. Duration of treatment was fifteen weeks; duration of the disease, twenty-three weeks.

Fig. 22. Miss M. T. (No. 34661), aged 28. Photograph June 15, 1936, shows recurrent multiple ulcers on the same leg after a fifteen-months' cure. Their duration was two weeks.

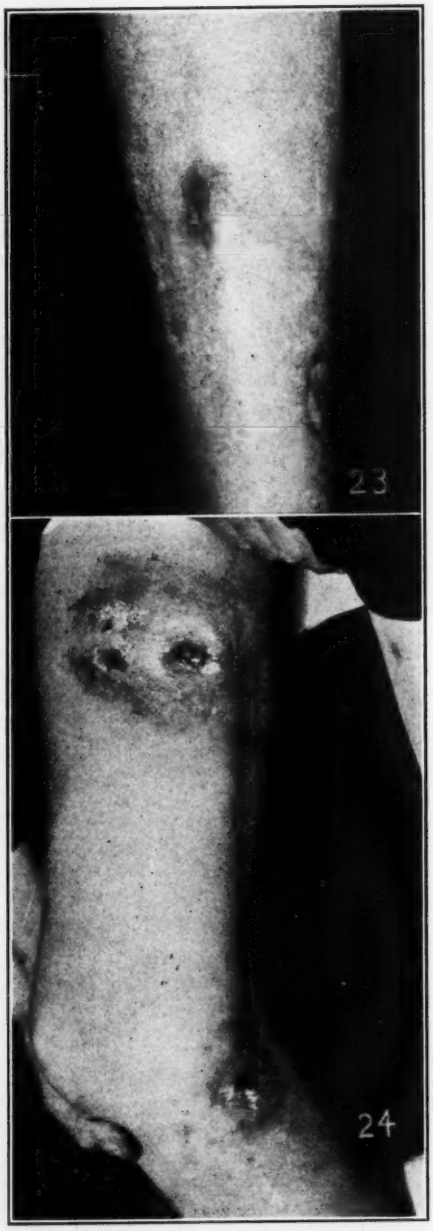

Fig. 23. Miss M. T. (No. 34661). Photograph July 22, 1936, shows healed ulcers. Duration of the treatment was five weeks; duration of the disease, seven weeks.

Fig. 24. Miss M. T. (No. 34661). Photograph June 15, 1936, shows multiple ulcers on the right thigh and leg (probably auto-inoculated) of ten days' duration.

quick and rapid destruction of the integument and subcutaneous tissues. Frank pus forms in the early stage, but when drainage is established the discharge becomes serous or sero-purulent. Blind sinuses and undermining of the skin may be considered characteristic findings in this disease. A honey-combing of the subcutaneous tissue by the infection results in multiple, small ulcers which form several centimeters away from the parent ulcer. These daughter ulcers rapidly enlarge by the melting away of the skin in the wake of the infection. The margins of these secondarily formed ulcers likewise become undermined.

The writer has not had the opportunity to attempt to produce the disease in the human being, but was successful in producing it in rabbits and recovering the micro-organism in pure culture. Castellani, in 1927, successfully reproduced the disease in a human volunteer.

Its pathogenicity for lower animals appears to be low. Results of attempts at producing

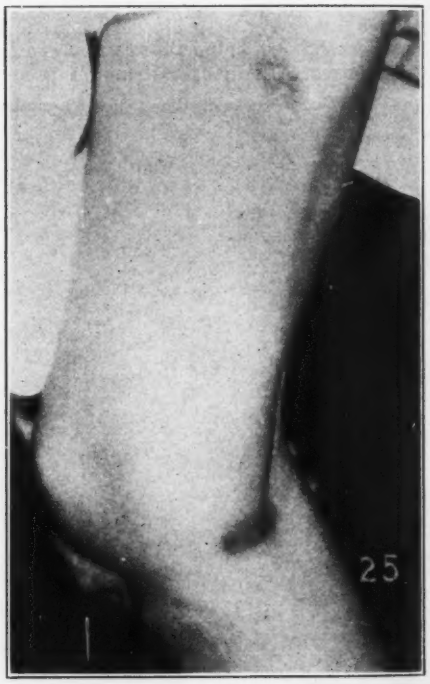

Fig. 25. Miss M. T. (No. 34661). Photograph July 22, 1936, shows the healed ulcers. Duration of treatment was five weeks; duration of the disease, seven weeks.

ulceration in rabbits and guinea pigs have been inconsistent.

The stubborn resistance of this lesion to any form of therapy taxes one's ingenuity and patience (*Table 4*).

As stated above, the clinical findings in many patients appear trivial, especially to one without experience in treating the affection. The ulcer may be healing nicely, in fact be almost well, when within a few hours it may be found to have

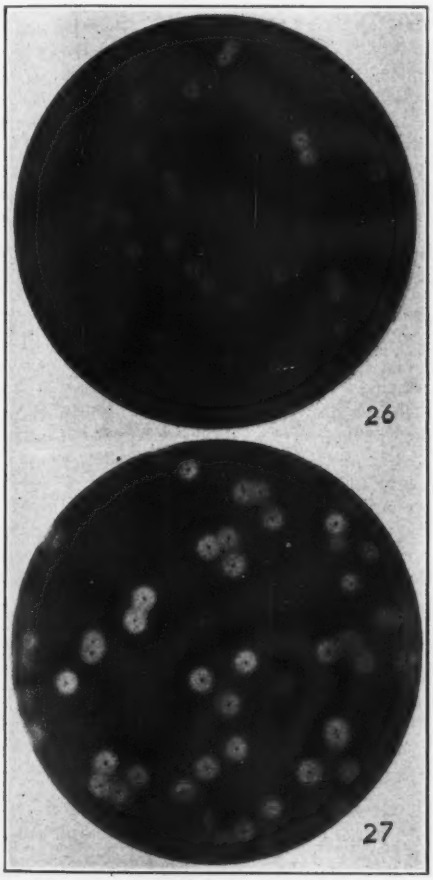

Fig. 26. Photograph of an aerobic, hemolytic blood agar plate culture from ulcers of Miss M. T. (No. 34661). Note the dense center and translucent, granular border.

Fig. 27. Photograph of an anaerobic, hemolytic blood agar plate culture from the ulcers of Miss M. T. (No. 34661). Note the dense center and faintly visible granular, translucent border about the colonies at the bottom of the media. Hemolysis is more marked than in Fig. 26.

Fig. 28. Mr. W. L. S. (No. 26922), aged 20. Photograph January 17, 1931, left leg, shows one of the original ulcers near the ankle and multiple ulcers along the site of surgical incision. The duration was six months. Following a blister on the heel, extensive cellulitis of the leg with systemic reaction occurred. The leg was widely incised. Subsequently numerous ulcers appeared with contracture of the knee. Pinch grafts applied elsewhere were unsuccessful.

Fig. 29. Mr. W. L. S. (No. 26922). The photograph shows the healed ulcers. Duration of the treatment was three and a half months; duration of the disease, nine and a half months.

Table 4

RESISTANCE OF MICROCOCCUS MYCETICUS TO TEN MINUTES' EXPOSURE TO CHEMICAL AGENTS

Chemical	Growth in
Mercurochrome	1-100 and up
Silloid crystals	1-100 and up
Silver nitrate	1-1000 and up
Metaphen (tr.)	1-1000 and up
Potassium permanganate	1-2000 and up
Bichloride	1-2000 and up
Phenol	1-4000 and up
Merthiolate (tr.)	1-4000 and up
Cysteine hydrochloride	1-4000 and up

enlarged and involved much of the previously healed tissues. This was of more frequent occurrence among our earlier patients.

Many different chemicals and modalities have been used in our attempts to cure the infection. We are still in search of an agent that will be most effective in eradicating the infection. Among the remedies used in treating the condition may be mentioned vaccines, potassium permanganate, Dakin's solution, hydrogen peroxide, urea, cysteine hydrochloride, silver nitrate, merthiolate, metaphen, lenigallol, mercurochrome, silloid crystals, methyl violet, gentian violet, concentrated nitric acid preceded by phenol, x-ray irradiation, heliotherapy and alpine lamp. An occasion has not arisen to permit the use of the more recently developed chemicals, zinc peroxide and sulfanilamide, but they will be given a trial when an opportunity presents itself.

The most effective therapeutic regime we have found is as follows:

(1) Absolute bed rest, if possible.

(2) If the ulcer is very dirty with adherent crusts the crusts are removed and fresh urea solution applied for one to two hours three times daily, changing the dressings often. This is applied continually until the ulcer is clean. Dry heat is applied in the intervals.

(3) If the ulcer is clean we use potassium permanganate, 1:1500 dilution, as a wet dressing continuously for the first 48 to 72 hours, then alternately with other agents. During the day a fresh solution of 0.5 per cent cysteine hydrochloride is applied to the ulcer for one hour, alternating with dry heat three hours. It must be remembered that every patient is an individual unto himself and no hard and fast therapeutic plan can be followed. The disease is hard to cure at best.

The patients who give us most concern are those with the undermining, burrowing type of ulcer. We have seen the undesirable effects of surgery performed on these patients before as well as after admission to the Clinic, which has caused us to shrink from this procedure, although surgery must be resorted to in some cases in order to make other therapy more effective. The admonition is that as little surgery be done as possible and as a last resort measure; that the diagnosis be established, if possible, before the scalpel is used.

If skin grafting is contemplated it can be done with safety only after a number of bacterial counts have been made in which no gram-positive or gram-negative intracellular diplococci are found in the ulcer. If these cocci are present in the ulcer when the grafts are applied many, if not all, of the grafts will probably be destroyed. This has happened repeatedly.

There have been only two recurrences and these were in patients with bilateral involvement of the legs. The others have remained well. Following incision of a skin flap overlying a sinus, constitutional symptoms of concern were observed in one patient. Rapid extension of the infection was accompanied by a temperature of 103.6°. No deaths have occurred from the infection *per se*. The morbidity rate, however, as shown in *Table 5*, is appallingly high for a lesion which apparently is insignificant and trivial. The shortest duration for the disease for the 44 patients was 4 weeks; the longest ten years; the average 13½ months. Only 21 of the 44 patients were hospitalized. Treatment was outlined for the others to be carried out at home. The shortest duration of the treatment was 2 weeks; the longest 14½ months; the average 2.7 months.

CONCLUSIONS

(1) Pseudomycosis due to *Micrococcus myceticus* is believed to be a definite disease entity which was first described by Castellani in 1928.

(2) A total of 54 patients with this disease have been studied since seeing the first patient in December, 1927.

(3) Historical, laboratory and clinical data of 44 patients are recorded in this paper.

(4) To minimize errors, close cooperation between the physician and the laboratory personnel is essential.

(5) Skin grafts are not advised so long as *Micrococcus myceticus* can be recovered from the lesion.

(6) Surgery should be reduced to a minimum

Table 5

COMPOSITE ANALYSIS OF 44 PATIENTS WITH PSEUDOMYCOSIS

	No.	Patient	Age	Admit.	Duration on Admission	Culture	Duration Treatment	Total Dura. Dis.	Result
1	23091	S.A.B.	50	4/16/29	3 weeks	Pure	4 weeks	7 weeks	Cured
2	05684	A.G.	11	6/12/29	8 months	Mixed	14½ months	23 months	Cured
3	24930	E.B.	12	2/22/30	6 weeks	Mixed	2 months	3½ months	Cured
4	25518	R.P.J.	22	6/ 2/30	3 weeks	Mixed	3 weeks	6 weeks	Cured
5	26102	A.S.B.	49	8/29/30	16 months	Pure	6 weeks	17½ months	Cured
6	26410	L.J.	53	10/14/30	6 weeks	Mixed	4½ months	6 months	Cured
7	26922	W.L.S.	20	1/17/31	6 months	Mixed	3½ months	9½ months	Cured
8	27275	N.D.	12	3/23/31	2 days	Pure	5 months	5 months	Cured
9	27518	J.M.	32	4/29/31	5 months	Mixed	1 month	Unknown	Cured
10	28072	B.S.M.	44	7/20/31	2 months	Mixed	1½ months	3½ months	Cured
11	28211	E.B.	33	8/11/31	1 month	Mixed	3 weeks	7 weeks	Cured
12	28607	J.A.C.	48	10/16/31	24 months	Pure	2½ months	26½ months	Cured
13	22673	N.V.R.	30	11/19/31	4½ months	Mixed	6 weeks	6 months	Cured
14	28935	J.R.W.	14	12/14/31	7 months	Mixed	5 months	12 months	Cured
15	28945	C.L.	17	12/15/31	3 months	Pure	4½ months	7½ months	Cured
16	29297	B.B.H.	23	2/26/32	9 months	Mixed	3 months	12 months	Cured
17	29361	A.W.	40	3/ 9/32	2 weeks	Mixed	9 days	4 weeks	Cured
18	29685	L.C.P.	18	5/19/32	7 months	Mixed	2½ weeks	7½ months	Cured
19	29902	A.D.	30	6/28/32	8 months	Mixed	2½ months	10¾ months	Cured
20	30233	L.B.	23	8/24/32	3½ months	Pure	4 months	7½ months	Cured
21	05504	J.A.S.	16	9/ 5/32	2 weeks	Mixed	7 weeks	2¼ months	Cured
22	30740	B.S.	21	11/16/32	11 days	Mixed	7 weeks	2¼ months	Cured
23	31696	L.B.M.	29	5/22/33	15 months	Mixed	2¼ months	17½ months	Cured
24	32511	N.B.K.	28	10/10/33	1 day	Mixed	1¾ months	1¾ months	Cured
25	33818	M.P.	13	5/30/34	2½ months	Pure	13 months	15½ months	Cured
26	34446	I.P.	12	9/11/34	4 months	Mixed	6½ weeks	5½ months	Cured
27	05791	M.E.	18	9/22/34	24 months	Mixed	2 months	26 months	Cured
28	34661	M.T.	27	10/ 6/34	2 months	Mixed	3½ months	5½ months	Cured
29	05753	P.B.	11	12/13/34	18 months	Mixed	2 months	20 months	Cured
30	35369	J.K.M.	56	2/ 4/35	16 months	Mixed	8 months	24 months	Cured
31	36766	H.H.	20	8/29/35	3 months	Mixed	1 month	4 months	Cured
32	36822	R.K.	28	9/ 7/35	1 month	Mixed	3 months	4 months	Cured
33	36885	J.E.F.	17	9/17/35	2 days	Mixed	4 months	4 months	Cured
34	37397	E.H.	14	12/ 3/35	13 months	Pure	4 months	17 months	Cured
35	38529	A.J.	44	6/ 2/36	120 months	Mixed	4 months	124 months	Cured
36	39081	E.J.	26	8/10/36	1 month	Mixed	2 months	3 months	Cured
37	38065	L.E.H.	43	9/11/36	1 week	Pure	3 weeks	1 month	Cured
38	37861	K.W.	21	3/ 2/36	6 months	Mixed	16 days	6½ months	Cured
39	36390	S.D.	26	7/ 8/35	3½ months	Pure	½ month	4 months	Cured
40	28270	L.L.W.	10	7/13/35	1 month	Pure	¾ month	1¾ months	Cured
41	39409	P.C.	36	9/19/36	48 months	Mixed	1½ months	49½ months	Cured
42	37997	E.B.	14	3/19/36	1½ months	Mixed	½ month	2 months	Cured
43	41698	P.M.	67	8/17/37	36 months	Mixed	1 month	37 months	Cured
44	31240	I.B.	14	2/22/33	36 months	Pure	2 months	38 months	Cured

because it predisposes to the spread of the infection.

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ARTHUS'S PHENOMENON FROM MOSQUITO BITES*

REPORT OF A CASE WITH EXPERIMENTAL STUDIES

By ALAN BROWN, M.D.
T. H. D. GRIFFITTS, M.D.
STANLEY ERWIN, M.D.
and
LUCIEN Y. DYRENFORTH, M.D.
Jacksonville, Florida

The phenomenon of Arthus has rarely been reported, a search of the literature revealing but thirteen cases. In 1902, Richet[1] discovered that if sublethal doses of the poison from the tentacles of the sea anemone were injected into dogs and from three to five days later the same dose, or even a smaller one, was repeated, the animals died promptly following respiratory difficulty, vomiting and diarrhea. This phenomenon, so at variance with the protection of antitoxic immunity, he termed anaphylactic reaction. The next year, Arthus,[2] in elaborating on Richet's work, discovered that any foreign protein might produce general anaphylaxis if injected intravenously after a suitable period for the establishment of sensitization. If the second injection was made subcutaneously, shock was absent, he observed, the reaction being localized at the site of the injection and varying from inflammation to necrosis. This reaction was called local anaphylaxis or the phenomenon of Arthus. In further pursuing these studies, von Pirquet,[3] with his explanation of serum sickness, formulated the original concept of allergy, namely: the changed reacting ability of the body due to antibodies or reagins.

Lucas and Gay,[4] in 1909, described local anaphylaxis occurring in children following reinoculation with diphtheria serum. Since then Péhu and Durand,[5] Gatewood and Baldridge,[6] Tumpeer and his co-workers,[7] Irish and Reynolds,[8] Maroney,[9] and Ross[10] have reported Arthus's phenomenon in human beings following reinoculation with antigenic sera containing the same antibodies or from different antigenic sera from the same animal source. In 1934, Gratia and Gilson[11] attributed postoperative complications to Arthus's phenomenon from catgut sutures.

In the case here presented, the causative agent was *Aedes aegypti,* a household mosquito common in the southern states. This report of skin necrosis in the human resulting from mosquito bites is apparently unique in the literature.

REPORT OF A CASE

A white girl, aged 15, a native Georgian who had resided continuously in Georgia and Florida, came under our observation on November 8, 1934, because of a skin condition of long standing, caused, she and her father said, by mosquito bites. The formation of blebs, varying in size from a pea to a half-dollar but without subsequent necrosis and scarring, was first noticed when she was 2½ years old. The size and duration of the blebs had gradually increased, and five years later it had become apparent that mosquito bites invariably induced swelling which lasted from five to seven days and involved an area having a diameter of from one to two inches about the site of the bite. Necrosis of the inoculated area had accompanied the process since she was 9 years of age, the formation of blebs being superseded by predominance of the necrotizing phase and the production of scars. In 1930 the swelling of the arms and legs from multiple mosquito bites had persisted well into the fall and was accompanied by a hardness of the tissues, formerly absent. Thereafter the seasonal swelling coincident with the mosquito season had lasted longer each season, and the induration had become more marked and persistent after the disappearance of mosquitoes.

Several physicians of another city had examined the patient. Skin tests for numerous plants and weeds had all been negative, and various diets and long use of cod liver oil had been without benefit. For six months in 1928 she had been given generalized ultraviolet radia-

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tion with exposures lasting up to fifteen minutes; blisters did not occur. The next summer she had been given at weekly intervals small injections of sulpharsphenamine for three months followed by large injections for a like period. The disease had remained unaltered.

History.—The patient was born January 23, 1919, full term, normal delivery, and was breast-fed for eleven months. Diseases of childhood were whooping cough, mumps, measles, "pink eye" and chicken pox. In addition to the skin abnormality, there was a history of menstrual irregularity, from three to five months elapsing between menses. The family history showed no known tuberculous infection. The maternal great-grandfather had had asthma, as had several of his children by his first wife and one of several by his second wife. His daughter, the patient's maternal grandmother, had sick headaches and two of her daughters had hay fever. The patient's mother, however, was free from allergic manifestations, as were the siblings up to that time.

Physical Examination.—Upon admission of the patient to St. Luke's Hospital, Jacksonville, Florida, the internist's examination showed smallness of stature, infantile genitals, reduced development of secondary sex characteristics and early closure of the epiphyses. Showing the physical development of a 13-year-old girl, she was considered as having a pituitary and thyroid insufficiency. There was brawny edema of the forearms, hands, lower legs and feet with pitting on hard pressure; the skin of the ankles was thickened, dry and warty. The edematous areas showed patches of inflammation, depressed areas of blue-black necrosis and pitted scars. On the face and trunk there were fewer pitted scars and no edema or inflammation.

Fig. 1

Within the circle on the right arm are shown experimental bites during the early necrotizing stage. Later necrosis from an adventitious bite is shown on the left hypothenar prominence. Over the proximal joint of the right little finger is shown an adventitious lesion after separation of the necrotic plug. The reduced amount of inflammation present was practically constant during the winter months.

Laboratory Data.—Blood chemistry determinations were:

Cholesterol	195-175-211
Sugar	80
Urea	29
Urea nitrogen	14
Nonprotein nitrogen	30
Uric acid	3
Calcium	11
Phosphorus	4.6
Chlorides	480
Creatinine	1.09
Icterus index	7.5 and 15

Except for cholesterol, which ranged from 175 to 211 mg. per 100 c. c. of blood, these determinations were within normal limits. The icterus index of 15 on August 9, 1935, was probably coincident with the occurrence of a subclinical malaria infection (benign tertian).

The Kahn test was negative. Three blood cultures were negative up to 14 days. At one time the erythrocyte count was 3,680,000, the leukocyte count 3,600 and the hemoglobin estimation 86 per cent; later the erythro-

Fig. 2

This picture was taken in the late fall when the inflammation was reduced to a degree that remained almost constant during the winter months.

cyte count was 4,230,000, the leukocyte count 7,100 and the hemoglobin estimation 87 per cent. While the erythrocyte count and hemoglobin value showed a mild anemia, the leukocyte and Schilling differential counts varied with the extent of the pyogenic skin processes. The Schilling index follows:

	8/9/35	1/10/36	2/27/36
Segmented cells	21	7	19
Stabs	8	21	15
Juveniles	0	2	8
Eosinophils	2	3	0
Basophils	0	0	2
Lymphocytes	69	66	54
Monocytes	0	1	2
	100	100	100

The clot retraction time was normal; the clotting time was 4 minutes and 10 seconds; and the bleeding time was 2 minutes. The platelet count decreased to normal and the fragility test showed hemolysis beginning at 0.40 per cent to 0.36 per cent. Benign tertian malaria parasites, *P. vivax,* were found on August 8, 1935.

Nocturnal search for filaria was negative. Urinalysis was repeatedly negative except for albumin, which ranged from a slight trace to 2 plus. Examination for hippuric acid showed 3.37 gms. for 1,555 c. c. of urine (24-hour output). The basal metabolic rate was zero and minus 7. Intradermal tuberculin tests were negative on two occasions.

Smears and cultures made repeatedly from the characteristic skin lesions showed a constantly recurring *Staphylococcus aureus,* accompanied by occasional streptococci, which were regarded as incidental. Skin tests made with twenty-two common antigenic substances were negative. Roentgen studies gave no evidence of bony involvement nor of pathology in the chest. The Shwartzman phenomenon was absent.

Experimental Studies.—When the patient was feeling well and her temperature normal, three female mosquitoes, *Aedes aegypti,* confined in drinking glasses with gauze tops, were allowed to bite her, two bites each on the right shoulder, over the left scapula and on the right forearm. Wheals appeared immediately and were surrounded directly afterward by erythematous zones; both rapidly increased in size, the wheals being from 2 to 15 mm. in diameter, irregular in shape and having pseudopodia, the zones varying from 1.5 to 6.0 cm. in diameter. Within two hours the lesions had disappeared except for the wheals, which contracted to diameters not exceeding 2 mm. Twenty-four hours after being bitten the patient was listless and complained of a frontal headache, also of "feeling chilly;" her pulse rate was 110 and her temperature 102° F. No erythema was present, and the wheals appeared to be progressing to blebs. After forty-eight hours she appeared even more indisposed, although her pulse rate was 96 and her temperature 99.3° F. Some blebs had developed, and other areas had assumed a deep purplish color. Scattered irregularly over the original erythematous zones on the edematous forearm were some grouped thin-walled vesicles resembling frog spawn. On the third day the patient looked and felt well, her pulse and temperature were normal; the purplish areas had increased in size and were less clearly marginated.

Depressed and darker on the fifth day, the purplish areas were by the eighth day slightly enlarged, the vesicles having dried and formed crusts; on the fourteenth day they were black with the centers separating from the adjacent skin by central contraction; and on the seventeenth day one of the necrotic plugs had separated, leaving a pea-sized cavity. During the following two weeks the necrotic tissue separated and all the experimental lesions healed, leaving depressed scars resembling large pock marks.

When the patient was several times subsequently caused to be bitten by *Aedes aegypti,* malaise and fever invariably followed, usually on the day after the bites. The immediate reactions tended to become larger, the wheals attaining diameters of from 1.5 to 2.5 cm. and the erythematous zones of from 5 to 8 cm., but they seemed to shorten in duration, disappearing entirely in ninety minutes. The formation of blebs and vesicles became less prominent and the necrosis was perhaps slightly greater in extent.

Experimental bites with *Culex quinquefasciatus* caused a smaller wheal than those from bites of *Aedes aegypti,* but a larger erythema, both of which faded in shorter time; also, the necrosis was less severe, causing a smaller scar. Bites of *Aedes taeniorhynchus* caused less immediate reaction, which promptly disappeared, and the scar from the necrosis was only 1.5 mm. in diameter.

The patient was subjected to intradermal injections of distilled water, normal saline, dilute moccasin venom, dilute rattlesnake venom and dilute formic acid solution. Her reactions were no greater and in some instances less than those of the control.

While under our care she had three attacks of erysipelas with rapid pulse and fever. Heavy exposures of ultraviolet radiation to the affected part resulted in prompt clinical response with no local reaction to suggest hydroa aestivale, a diagnosis made previously elsewhere.

Glycerinated extracts of *Aedes aegypti* and of *Culex quinquefasciatus* in several dilutions were prepared by the National Institute of Health, United States Public Health Service, for attempted desensitization. They were of two series, each containing equal numbers of the two species. One series was made from the dissected salivary glands, the other from the mosquitoes from which the glands had been removed. The two vaccines were given intradermally daily in ascending doses starting with 0.05 c. c. of extract equal to one-millionth of a mosquito gland, or mosquito body, per cubic centimeter. Thirty-six injections of each type of vaccine were given, the last ones representing 1.5 salivary glands or mosquitoes minus the glands. Each injection caused an inflammatory wheal, possibly due to the glycerin in the extract. As the dose increased, necrosis similar to that occasioned by the bites of mosquitoes became apparent. This reaction was, however, never as great in extent and lacked the accompanying malaise and fever; also, the resultant scars were but from 1.5 to 2 mm. in diameter, and the reactions to the vaccines were approximately parallel and equal. Following this attempt at desensitization an experimental bite provoked a necrosis of less extent than formerly, but benefit from these first vaccines was only temporary.

Subsequently, desensitization was attempted with a sterile saline extract of whole *Aedes aegypti,* injected subcutaneously daily. Because of a local inflammatory reaction the dose had to be reduced to an infinitesimal

quantity representing five one-thousandths of a mosquito, but was gradually increased to twenty-five one-thousandths, the maximum tolerated. As it was found impossible to prevent occasional adventitious bites, which might prevent desensitization, to nullify their effect an injection of 0.5 c. c. of epinephrine solution was ordered as soon as possible after their occurrence. On May 7, 1936, the patient received three bites from unidentified mosquitoes in less than a minute, and within two minutes thereafter the epinephrine was injected. She did not suffer the customary malaise and her maximum temperature was 99.8° F. The late reactions to the bites consisted of minute necrotic centers surrounded by small areas of capillary hemorrhage, this last a new phenomenon, and only minute scars remained.

The injection of epinephrine with the mosquito extract then minimized the local reaction, permitting larger dosage. After the administration of six ascending doses the patient was bitten experimentally by *Aedes aegypti* and epinephrine injected immediately after with a resulting decrease in local reaction, necrosis and scarring. The attempt to desensitize by the biting in conjunction with epinephrine was continued, but she became progressively nervous from the injections of epinephrine and they seemed to lose their protective power. Ephedrine was also administered orally, but the protective effect was not sufficient, although the reaction to it was definite. The efforts at desensitization were not successful and were at this point unavoidably discontinued.

Owing to the consistent recovery of *Staphylococcus aureus* from the bite lesions and the necrosis following injections of vaccine, the patient was given at three-day intervals eighteen injections of an autogenous vaccine of this organism, both to immunize her and to rule out or minimize the role of infection in the necrotic lesions. No change in the lesions could be discerned.

As a means of establishing an allergic mechanism as the cause of the bizarre reaction, a study of eosinophilic phenomena was made. Following a complete blood count the patient was bitten by mosquitoes and blood counts were repeated at intervals of five minutes, one hour and twenty-four hours from the time of biting. The eosinophilic percentages of the four counts were respectively three, five, none and one, showing an early rise of some significance which promptly disappeared.

COMPARATIVE BLOOD COUNTS

	Before Bites	5 Min. After	1 Hour After	24 Hours After
W. B. C.	7,100	7,950	7,200	5,600
R. B. C.	3,950,000	3,930,000	3,810,000	3,790,000
Hgb., per cent	76	76	73	71
Diff.				
Polys.	30	17	31	50
Juv.	2	1	4	3
Stabs	21	11	22	41
Segs.	7	5	5	6
Lymphs.	66	76	67	45
Eosin.	3	5	0	1
Monos.	1	2	2	4

Studies of biopsies from lesions caused by the bites showed eosinophilic infiltration into and about the necrotic areas, an essential point in the pathologic diagnosis of an allergic reaction.

The Prausnitz-Küstner reaction was attempted. It consists of the passive transference of allergic susceptibility by the intradermal injection of the blood serum of the patient into a control subject; the injected area and a normal area of the skin of the control are then injected with the suspected allergin and the reactions compared. If the test is positive, the reaction at the site of injection with the patient's serum will be altered. Twice this test was performed on one of the authors with negative results. It was then learned that allergic persons are unsuitable subjects as controls, and the test was repeated on two non-allergic subjects, both of whom gave similar positive reactions.

The test on T. H. D. G. is here described. On January 27, 1936, injection was made of the patient's blood serum into his skin in the flexor surface of the forearm, and two days later he was bitten by an *Aedes aegypti* on the previously injected area and on the arm three inches away. A wheal, appearing immediately on the injected area, attained a diameter of 12 mm. in fifteen minutes, and the erythematous zone surrounding it was 4 cm. in diameter at the end of thirty minutes. On the normal skin the wheals were 5 mm. and the erythema 11 mm. in diameter. Three hours afterward, the areas injected with the serum were sore to touch and slightly elevated; the erythema was 11 mm. in diameter. The bites on the normal skin had disappeared. The late phenomena with blebs and necrosis did not occur.

The reverse of the foregoing reaction was also attempted. The intradermal injection into the skin of the patient of the blood serum of a person whose reaction to bites of *Aedes aegypti* was a moderate immediate wheal was followed by bites of this species of mosquito on the prepared and unprepared skin. The prepared area showed a reaction of two wheals 2.5 mm. in diameter and an erythematous zone 5 by 8 cm. in extent. The two wheals on the unprepared skin rapidly became confluent with pseudopodia, the combined wheal becoming 1.5 by 2 cm. in dimension, and the erythematous area equaled that of the prepared area. All these bites went on to necrosis, but the prepared area showed less reaction at all times and less necrosis. This positive but partial protection, immunological in character, was not obtained by Hecht.[12]

To improve her general condition, regulate the scant and infrequent menses and promote the growth of secondary sexual characteristics, the patient was placed on a diet high in carbohydrates and given thyroid medication orally and injections of anterior pituitary-like sex hormone. The results were gratifying. Her weight increased from 75 to 93 pounds. Menstruation approached normal, and there was development of the mammae and increased growth of pubic hair. Her color was better. She appeared more alert mentally and had increased vigor. Unfortunately, a gluteal abscess of staphylococcic origin developed following an injection of A.P.L. sex hormone and deprived her of most of this gain. This medication was stopped and menstruation ceased.

Subsequent History.—Early in July, 1936, the patient moved with her family to Atlanta, Georgia. At that time she was in fair health and when seen by one of the authors in Atlanta the following September she was well and anticipating entering school a few days later. That fall she was forced to discontinue school because of a swelling of the abdomen. She afterward developed jaundice and became fatigued easily. Admitted to the Grady Hospital on February 25, 1937, she grew progressively worse. The passage of bloody stools began on March 5 and on March 9, 1937, she died.

Autopsy Findings.—Dr. Warren B. Matthews performed an autopsy. The significant postmortem findings were hypertrophic cirrhosis of the liver with marked fatty changes, splenomegaly due to chronic passive congestion, ascites, jaundice, marked anemia and intestinal hemorrhage due to multiple petechiae of the mucosa. To quote from the autopsy protocol "The lungs * * * are as nearly normal as lungs ever are on the autopsy table." Dr. Matthews' diagnosis was Hanot's cirrhosis, a rare and little understood condition.

An extensive literature on insect bites has accumulated in recent years, mostly in German medical journals. The most comprehensive writer has been Otto Hecht[12] of the Institute of Marine and Tropical Medicine of Hamburg. He stated that the reaction provoked by the bite of an insect is caused by the injection of salivary fluids; the toxic substance is not confined to the salivary secretion, but is extractable to a greater or lesser degree from other organs. The initial bite of some insects does not provoke a reaction, he found, but after a suitable period for the establishment of sensitization, subsequent bites provoke a toxic reaction; this reaction may be immediate wheal formation, delayed papule formation or both. The susceptibility of a person to a given species of insect is not constant, he observed, but may increase or decrease as evidenced in the size of the lesion, the intensity of the subjective symptoms, the duration of the reaction and the variation in the latent period before the appearance of the reaction. He performed the reverse Prausnitz-Küstner reaction by injecting a person who reacted to insect bites with the serum of a non-reacting person and then causing him to be bitten. The reaction to the bite was unchanged. Thus no local passive immunity, such as occurred in our case, was conferred. Hecht[12] concluded that the immediate wheal formation from insect bites is allergic in character, the delayed reaction being of similar though unproven mechanism. The decrease in necrosis in our patient from partial protection from normal serum injected before the mosquito bites would lend evidence to the delayed reaction's being also allergic. Thus the bite of insects may be considered an allergic manifestation as the tuberculin test is now thought to be.

Genner[13] described bullous eruptions observed in ten cases, which he attributed to mosquito bites and called "eruption bulleuse saisonniere." Bode[14] described similar lesions in two sisters in Göttingen and cited a case in Holland reported by Siemens.[14] He considered *Culex pipiens* the causative insect in his cases and called the condition "culicosis bullosa." Unfortunately, no experimental bites were made to prove the role of insects.

A number of able men have diagnosed the unique case here presented as hydroa aestivale, papulo-necrotic tuberculide, a blood dyscrasia and a staphylococcic pyodermia. Since the lesions occurred more on the legs and arms than the face and blistering doses of ultraviolet light caused no similar lesions, the diagnosis of hydroa aestivale may be dismissed. The active lesions did not resemble a papulo-necrotic tuberculide in their evolution, scarring or distribution. The negative tuberculin tests, roentgen studies of the lungs and findings at autopsy would make this diagnosis untenable. We know of no blood dyscrasia that presents a similar picture, and studies of the blood showed no abnormality. Staphylococcic pyodermia may be less easily dismissed as repeated cultures of *Staphylococcus aureus* were obtained from the lesions in various stages. However, contamination of lesions with this organism is to be expected. An autogenous vaccine did not alter their appearance in this case, and experimental bites on surgically cleansed skin were unchanged although disinfection of the mosquitoes was of course impossible. A sterile mosquito vaccine caused similar though smaller lesions, which progressed through the characteristic evolution. Injections of this vaccine appeared the same whether or not the patient's skin was sterilized before needle puncture. In unsterilized skin, needle puncture failed to cause lesions.

In the opinion of Dr. William Allen Pusey, who saw the patient, this case was unlike any he had seen in his exceptionally long and full career; and his willingness to accept our diagnosis of Arthus's phenomenon from the bite of *Aedes aegypti* cannot be lightly dismissed. There was repeated and invariable demonstration of lesions occurring after experimental bites and progressing through characteristic and protracted evolution to typical scarring, and in a patient with a history of familial allergy. Both the type of lesion and its evolution were unaltered by autogenous staphylococcic vaccine, mosquito vaccine and improvement in general health from A.P.L. sex hormone, thyroid medication and diet. The early characteristics of this case from the onset to the seventh year, when the lesions were bullous and healed without scar formation, are similar to the reactions described by Genner[13] and Bode,[14] suggesting that it was a more aggravated manifestation of a similar phenomenon due to the bite of an insect, in this instance

Aedes aegypti. The positive Prausnitz-Küstner reaction would definitely place this case in the allergic category in respect to the immediate reaction which was altered in the suitable non-allergic subjects. To be sure, there was not the delayed reaction with necrosis which characterized the patient, and which Hecht[12] was unable to transfer in his experiments. Nevertheless, biopsies of the delayed reactions, when necrosis was in progress, showed eosinophilic infiltration indicative of allergy. The blood eosinophilia of allergy was present five minutes after mosquito bites had occurred. Partial protection from bites by the intradermal injection of a normal person's blood serum into the patient, the reverse Prausnitz-Küstner reaction, constituted a measure of local passive immunity. In the face of these facts we consider the case one of Arthus's phenomenon from bites of *Aedes aegypti,* a common household mosquito.

SUMMARY

The discovery of Arthus's phenomenon or local anaphylaxis and the scant literature reporting its occurrence in the human have been briefly reviewed.

A case of skin necrosis in a white girl caused by the bite of *Aedes aegypti,* a common household mosquito of the southern states, has been presented, and experimental work pertaining to it has been described.

Attempted desensitization was unsuccessful.

Partial passive local immunization was obtained.

Literature on insect bites pertinent to the case has been cited.

Facts have been marshalled to substantiate the diagnosis of Arthus's phenomenon from mosquito bites.

It is concluded that skin necrosis from mosquito bites is localized anaphylaxis or Arthus's phenomenon, that is, allergic.

This case of skin necrosis in the human from mosquito bites is believed to be the first presented in the literature.*

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DISCUSSION (*Abstract*)

Dr. G. E. Johnson, Ardmore, Okla.—The effect of mosquito bites on different individuals has always been a very interesting subject to me. On some they produce hardly any signs or symptoms; on others they produce a severe inflammation followed by papules, maculae and wheals, even resulting in small abscesses after a few days. I noticed this particularly when I first married my Tennessee girl and took her down into Mississippi bottoms and she was unfortunately bitten by mosquitoes. I should like to ask the essayist to explain this. I should also like to know why the same mosquito will cause malarial hematuria in a white person, often reaching the chronic stage and resulting in hemoglobinuria, when it seldom, if ever, affects the Negro.

I practiced medicine for eight years in Mississippi and never saw a case of malarial hematuria in a Negro, but saw many such cases in white people.

Dr. Howard Hailey, Atlanta, Ga.—Dr. Brown requested me to discuss this paper, as I have seen the patient at various times, for a period of years.

About ten or eleven years ago, this patient was presented informally to a group of dermatologists at the closing session of the Section on Dermatology and Syphilology when the Southern Medical Association met in Atlanta. It was the consensus of opinion that the patient had hydroa vacciniforme. Two years ago, when Dr. Brown presented this patient at the Southeastern Dermatological Association meeting in Jacksonville, the lesions on the skin had some of the characteristics of papulonecrotic tuberculides. I am still impressed by

the fact that these lesions predominate on the exposed parts of the body.

Very few cases of hydroa vacciniforme have been followed for a number of years.

If Dr. Brown and his co-workers are presenting this patient primarily as one of "Arthus's phenomenon from mosquito bites," I am reluctant to accept the diagnosis as presented.

I do not know that a patient suffering from hydroa vacciniforme has ever been exposed to the bites of the mosquito. Should another case of this uncommon disease, hydroa vacciniforme, come under my care, I shall observe the effects of bites from the mosquito in question. The location of this eruption, the constitutional symptoms, and the vaccination-like appearance of the lesions as shown in the slides presented by Dr. Brown, strongly suggest that the patient has hydroa vacciniforme, and that the toxin from the mosquito is the exciting agent of the lesions.

The father of Dr. Brown's patient attended my clinic recently. For some time he has been suffering with an extensive eczema of the dysidrotic type. I believe this child inherited a hypersensitiveness of the skin from her father.

Dr. T. H. D. Griffitts, Savannah, Ga.—To my mind, this very interesting case is beyond doubt a case of Arthus's phenomenon from mosquito bites. Further, the case has been more thoroughly studied and experimented with than any other case relating to insect-bite reactions which is reported in the literature now available. It is the first case of the kind in America so recognized, studied and reported.

This girl had gone from physician to physician and from clinic to clinic, always with the question raised as to a possible connection between mosquito bites and her skin and general condition. No one had attempted experimentation with mosquitoes until she applied to Dr. Brown for diagnosis and treatment. Any skepticism we may have had was soon dissipated after beginning the applications of mosquitoes. The exaggerated local reactions always immediately occurred, with the appearance of a wheal, followed by a pronounced macule, succeeding to necrosis and scar formation, and the accompanying general reaction for the first 24 to 48 hours. A natural assumption was that the exciting cause of the mosquito bite reactions in this girl was one of the house-infesting mosquitoes, so we applied at various times the two most prevalent "house mosquitoes" of the South, *Aedes aegypti* and *Culex quinquefasciatus*. It is generally well known that with practically all people the bite of *Aedes aegypti* is decidedly more irritating than that of other mosquitoes, and in this case there was observed the usual relative severity. However, necrosis, to less extent, occurred also after the bites from *Culex quinquefasciatus*.

Our attempts at desensitization by injections of extracts made from both whole mosquito bodies and from the salivary glands, while temporarily encouraging, proved, ultimately, of no permanent benefit.

The report of this case in detail may excite an interest in cases of this nature. It is hoped that dermatologists and others who may have occasion to take up similar studies will be sure of the species of mosquitoes with which they are dealing or with which they may conduct investigations, remembering that there are hundreds of different species and those prevalent in one section of the country may be quite different from others. In such cases as reported in the literature so far, as mentioned in the paper, there is a dearth of information bearing upon the species of mosquitoes or other insects concerned. Here we have definitely established a causative relationship between the bites of two species of mosquitoes, *Aedes aegypti* and *Culex quinquefasciatus*. Further attempts at desensitization with mosquito extracts should be made.

PRIMARY CARCINOMA OF THE LIVER*

TWO CASES ASSOCIATED WITH CIRRHOSIS

By LEE RICE, M.D., F.A.C.P.
San Antonio, Texas

During the week of August 16, 1936, two men from Mexico consulted me for abdominal discomfort, the first complaining of pain in the right abdomen. Both had enlarged livers, palpable tumors in the liver, slight jaundice, loss of weight, and the possibilities of cirrhosis, cancer, and amebic abscesses. The latter are not uncommon in the hot countries, and neither are they latent if careful examinations be made.

Primary cancer of the liver is rare, with only 360 to 370 proven cases in the literature, but there have been at least three times as many carefully observed cases, and I happen to know of five cases now with necropsy findings which have not been reported. Cirrhosis of the portal type is, however, very common, particularly in Mexico, where I recently saw twenty-seven men in one ward at Puebla with "pulque" cirrhosis, and syphilis is still prevalent in the hot countries of our Gulf Coast as a probable etiological factor. Typhoid fever followed by recurring digestive disturbances and constipation must be a probable cause of cirrhosis, and chronic malaria with frequent re-infection has to be considered along with chronic intestinal parasitic infections plus liquor or "pulque" or food deficiencies, or without them. If steady, or regularly intermittent, drunkenness causes a man to neglect his vitamins, I should not blame the latter, but I should strongly consider the so-called hang-over and the very toxic state of his entire body for the succeeding forty-eight hours as definite adjuvants to the alcohol that he had consumed in the gradual production of a chronic cirrhosis. The weight of clinical observation is so great that we may as well accept as a probability that about one-half of the cases of hepatic cirrhosis are produced by or associated with alcohol and its toxic reactions, and that 10 to 15 per cent are the result of syphilis. In more than half

*Read in Section on Gastroenterology, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

of the remainder the etiology is usually fairly clear, if we may accept often repeated intoxicants or intestinal parasites as causative factors, and since the liver is always enlarged, and rapidly changes in size and consistency in the early cases, the diagnosis can be made then and the patient may be successfully treated if the chronic intoxicant can be eliminated.

One has to be wary about a positive Wassermann in chronic liver disease, since about 50 per cent of the reported primary cancers and one of the cases reported here had positive Wassermann tests with no evidence of the disease at necropsy. Some substance is elaborated or is not eliminated by enlarged and chronic livers that disturbs the Wassermann test.

All observers are agreed that 80 to 87 per cent of patients with primary carcinoma of the liver also have cirrhosis of the portal, toxic or biliary types.

Case 1.—A retired ranchman of 51 years complained of right abdominal pain on August 13, 1936. He had pain of a similar nature for five days in June, and when the pain recurred on August 1, he feared appendicitis and started driving out of Mexico. He reduced his diet to liquids and had lost 30 pounds. The pain had been dull with no radiation and was not constant, no nausea, bowels regular, no urinary symptoms, no weakness, slight jaundice in July.

He had had typhoid fever in 1909, malaria several times, no intestinal parasites, and was a steady but moderate drinker. His tongue was heavily coated, there was no lead line, there was a slight yellow tinge of the sclera. His blood pressure was 124/88, heart and chest were negative. A large, firm, tender right lobe of the liver could be felt 6 cm. below the costal border, and a firmer, less tender tumor in the region of the gallbladder. The prostate was normal; there were no enlarged veins, no ascites, no hernia, and the spleen was not palpable. The Wassermann and Kahn were negative. Three urinalyses were normal. There was no bile. Two stools were negative. They were cultured for ameba. Duodenal drainage was done twice. There was a free flow, no ameba were detected, but the findings were essentially normal. A pure culture of *Staphylococcus albus* was found. Red cells were 4,130,000, hemoglobin 83 per cent, white blood cells 8,450, with 64 per cent segmented. Icterus index was 4. Dextrose tolerance was normal. There was no retention of bromsulphalein.

Complete radiographic studies, including the long bones, were entirely negative for both primary carcinoma and metastatic lesions.

The patient improved and on September 11 he had gained three pounds, was much better, and the liver was smaller and less tender. Fifty days later jaundice appeared and bile was found in the urine for the first time. Radiographic studies were again negative, and he was sent to the hospital on November 6. Again roentgenograms were negative and the gallbladder concentrated dye satisfactorily. The large central tumor could be outlined, and I had become convinced that it was a primary tumor, probably cancer. The prostate had remained normal and there were no enlarged veins.

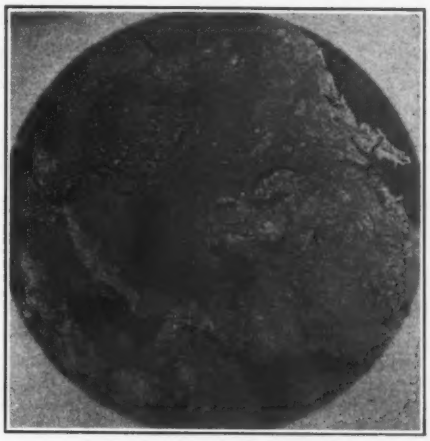

Fig. 1
Section of large solitary cancer in Case 1 obtained at operation. Advanced cirrhosis with invasion of the hepatoma is shown.

Dr. C. S. Venable did an exploration of the abdomen on November 17. A large carcinoma displaced the entire central third of the liver, had invaded the gallbladder, and was adherent to the omentum. The remaining portions of liver were streaked with grayish bands, nodular from cirrhosis, pigmented with bile and showing chronic passive congestion. Two enlarged and invaded nodes were found along the cystic duct, and all other viscera were normal. The borders of the tumor were sharply outlined and extended over the dome of the liver beyond our view. The biopsy sections showed cirrhosis and carcinoma (hepatoma) grade three (Dr. D. A. Todd).

The operation produced no reaction and the patient ate well until December 1, although jaundice was increasing. On that date the right diaphragm was perforated, pleural pain was annoying, and a small amount of fluid accumulated in the right pleural cavity. Three days later roentgenograms revealed small metastatic nodules in the right lower lobe above a small amount of fluid, and the left fornix was obliterated with fluid. Both pleural cavities filled rapidly and he expired on December 11, 1936.

An abdominal necropsy one hour after death revealed no invasion of any other abdominal viscera. The stomach was normal and the pancreas showed early atrophic changes. The prostate was normal. The liver was densely adherent to the right diaphragm, and the lower lobe of the right lung had been invaded. There were no nodules in the left lung, but the cavity contained about 300 c. c. of clear straw-colored fluid. Sections from the liver and the cancer again showed cirrhosis, moderately advanced, and carcinoma grade three (hepatoma).

It seems likely that this case may be accepted as a primary carcinoma of the liver with metastasis to the right lung and chronic portal cirrhosis produced by alcohol or malaria, or both.

Case 2.—A retired capitalist, aged 57, complained of abdominal discomfort on August 19, 1936, that had recurred frequently for six months, and during the previous week had been annoying in the epigastrium. He had lost 10 pounds, but had felt no weakness, and his appetite and bowels had been normal. He had noticed orange-colored urine once and had had no other symptoms. He had lived in Mexico twenty-five years and had had no real illnesses, except influenza eight years before. His drinking had been moderate as well as his smoking.

The tongue was slightly coated. There was no jaundice. His blood pressure was 134/88 and the heart sounds were regular and clear. The abdomen was normal excepting a large, firm, slightly nodular liver 5 cm. below the costal border. The rectum was negative. There were no enlarged veins. The prostate was soft and normal.

Red cells were 3,950,000, hemoglobin 80 per cent, white cells 9,050 with 67 per cent segmented cells. Wassermann, Kolmer and Kahn were 4 plus, icterus index was 6.6, four urinalyses were normal, with no bile. Three stools revealed neither ova nor parasites and no occult blood. Four duodenal drainages produced free flow. No amebas were detected and drainage seemed to induce some improvement.

There was a brief bout of temperature in October and November. During the latter, bile was found in the urine and the white blood cells were 13,350 with 77 per cent segmented forms. Three complete radiological studies had been negative, including visualization of the gallbladder.

For a period of four months potassium iodide was given by mouth, and bismuth and liver extract were given into the hip muscles each week. In January, 1937, a nodule in the middle third of the liver began to enlarge and roentgenograms of the stomach and chest were again negative, but I had become convinced that he had a carcinoma in the liver. I asked for consultation, and finally got him off to Dallas in March to see Dr. Henry M. Winans. After a week of study Dr. Winans could not confirm my diagnosis of cancer, saying:

"If primary, one would certainly expect jaundice by this time, and if secondary, from some place in the gastro-intestinal tract, especially the pancreas, he should have ascites. Of course he has neither."

Dr. Winans found the icterus index 7.5 and his glucose tolerance perfectly normal with no disturbance in the liver's ability to store the anti-anemic factor, since the red cell diameter was slightly below average. Hippuric acid synthesis was 2.27 grams.

On April 5, 1937, he was hospitalized and 500 c. c. of 10 per cent glucose in normal saline were given intravenously daily in accordance with Albert M. Snell's

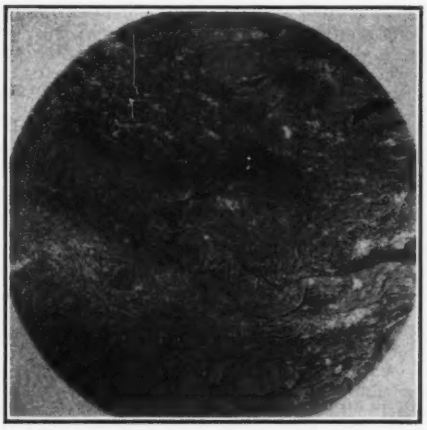

Fig. 3

Section of liver at necropsy in Case 2 demonstrating the columnar arrangement of cells. Dense strands of old fibrous tissue are being invaded.

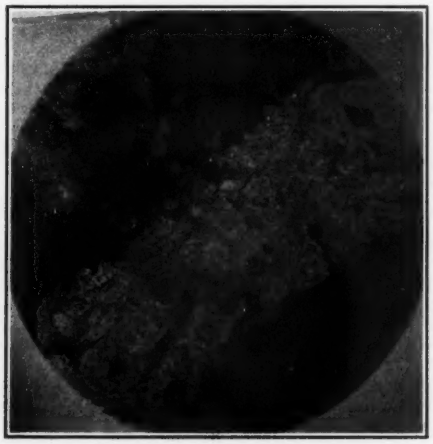

Fig. 2

Biopsy of liver in Case 2 obtained with sharp spinal needle, shows columnar arrangement of cells with tendency to form lobules.

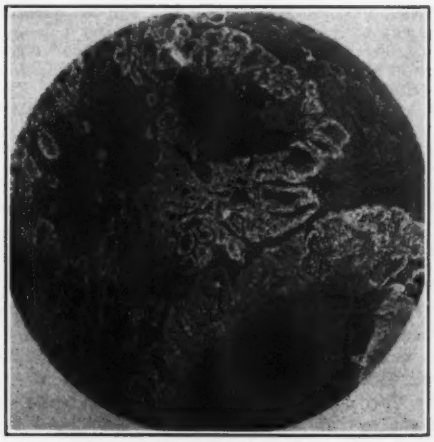

Fig. 4

Adenocarcinoma of stomach in Case 2 which was symptomless, but caused death from a massive hemorrhage.

Fig. 5

Shows the large liver in Case 2 with advanced cirrhosis and almost complete invasion by the hepatoma. All photographs by Drs. Lehman and Pipkin.

suggestion and because beneficial results had been obtained in several patients by his group at Rochester. Two days later biopsy specimens were obtained by quick strokes into the tumor mass with a sharp spinal needle, and at the same time the liver was carefully explored for an abscess or cyst. The specimens were numerous, and showed a carcinoma grade 3 (hepatoma).

Then complete radiograms were repeated with no evidence of metastasis. The lesser curvature of the stomach had become adherent and would not remain filled, but it could be filled smoothly under the fluoroscope.

For sixty days 500 c. c. of 10 per cent glucose in normal salt were given intravenously every morning, and small doses of x-ray were given as a palliative measure. He had no temperature, the blood count improved, there was no bile in the urine, and no blood in the stools. Every stool was examined for five months. He went home on June 1 and was out practically every day during the summer. His appetite was steadily good, and four pounds in weight were gained. Practically every afternoon he had a bottle of beer and a cheese sandwich with no symptoms of any kind. The bowels remained regular and only one enema was given throughout the summer.

On September 2 he had a premonition of death, and had a massive intestinal hemorrhage at 3:45 the next morning, followed by death four hours later.

Dr. D. A. Todd did the necropsy. The lungs were normal with no adhesions and no nodules. The right lung was compressed by the liver, which was at the level of the second rib. There was no lesion in either the heart or the aorta. The anterior abdominal wall and the entire right diaphragm were densely adherent to the liver, but neither had been perforated. The liver was replaced by a very large grayish yellow cancer with no liver tissue discoverable except a small 2 cm. strip along the extreme left border, and the mass weighed 5,600 grams. The pancreas was small and atrophic. Two thickened nodes were found near the head of the pancreas. The kidneys were slightly small. The spleen was twice normal size, the intestines moderately congested, and the prostate negative. The stomach was filled with blood, and as a saddle over the mid-lessor curvature lay a papillary adenocarcinoma moderately adherent to the liver. From this the hemorrhage had occurred and the esophageal veins were not remarkably dilated.

A careful search has revealed no evidence of syphilis. The liver tissue showed an advanced cirrhosis, and Dr. Todd thinks there is less than 10 per cent of liver tissue remaining. It seems unbelievable that he had no jaundice, no indigestion, no bile in the stools, and good fat digestion.

The pathologist is sure that the primary lesion was in the stomach, but another disagrees, and with no ascites and no symptoms, no anemia beyond that of the first examination, and a good appetite and slight gain in weight, I cannot accept it clinically, although it is certainly not a proven case of primary carcinoma of the liver.

In 1890 Von Hansemann reported four primary cancers of the liver, and Goldreiher and Von Bokay reported eighteen cases in 1910. Eighteen cases in 14,000 necropsies have been found at the Johns Hopkins Hospital, and in 1923 Clawson and Cabot found only one case in 5,100 necropsies at the University of Minnesota. Metastasis usually occurs in adjacent organs and often in remote. In February, 1937, Bolker, Jacobi and Koven reported a primary cancer of the liver with metastasis to the bone, and had found nine other similar cases in the literature.

Strong and Pitts reported 12 cases in 1932; 10 in Chinese and 2 in white men. One white man had no cirrhosis, but in a recent letter Dr. Strong said:

"We have continued to add to this series (1932 report in *Annals of Internal Medicine*). It is our impression that primary carcinoma invariably develops on a basis of cirrhosis, and we feel that in these Chinese, liver fluke infestation probably leads to a chronic hepatitis with subsequent cirrhosis and in some cases primary carcinoma."

In a recent letter Dr. Strong told me that the Vancouver General Hospital has now collected 30 cases of primary carcinoma of the liver, 9 in

whites and 21 in orientals, and that all had well-marked cirrhosis.

"The clinical picture was that of rapidly progressing cirrhosis with ascites."

Hill reported 4 cases from San Antonio in 1925. Three had positive Wassermann tests, one had syphilis, and all had cirrhosis. He thinks a primary cancer of the liver should show a basic cirrhosis, and is never surprised to find a positive Wassermann with no evidence of syphilis.

The positive Wassermann offers a problem in diagnosis that misled me, and through me, a consultant in one case. If the cirrhosis be advanced, specific treatment must be given carefully, and may cause further trouble. It is, at least, well to remember that there may be no syphilis in any given hepatic cirrhosis, and the test might even lead one to suspect primary carcinoma in one-half of the patients with "cirrhosis and liver tumor."

What might be done about the earlier recognition of cirrhosis of the liver and its probable cure, before, as Snell and Rowntree say, the liver becomes decompensated? Or before 0.15 per cent of primary carcinomas develop as recorded in most necropsy reports, which would probably be at least 2 per cent in cirrhotic livers if they were grouped separately. Snell and his associates feel that a great deal can be done. They rely on a very careful history and liver tests in diagnosis, with the proven benefits of a high carbohydrate-low protein (or low meat) diet following the elimination of all intoxicants. I think they have now proven that glucose intravenously has actually cured moderately advanced cirrhosis. Sprunt, of Baltimore, said that

"a high carbohydrate diet is essential. This is the most important single agent that we possess that may be conducive to building up the liver's resistance and adding to its reserve. Our ideal should be to keep the liver cells constantly well supplied with glycogen."

He referred to Forbes, Neale and Sherer's description of an aqueous solution of their alcoholic fraction of liver that protects animals against necrosis from chloroform or carbon tetrachloride administration. Clinical experiences have certainly indicated the apparent and occasionally striking benefit of liver extract in serious disease of the liver.

All observers have noted the frequency of cirrhosis in primary cancer and have reported its incidence as 83, 87, and even 100 per cent. Cirrhosis is so common that it may be an incident or a causative factor, but it is, at least, a condition that can be suspected and successfully treated in its early and even far advanced stages.

About 10 per cent of men 40 years or older who complain of abdominal discomfort have enlarged livers. Unless there be tenderness along the liver border or in the region of the gallbladder, little attention is paid to the simple, even enlargement, but many, if not all of these livers, are passing through the early stage of cirrhosis, and one should not wait until the liver becomes nodular and ascites is evident to make the diagnosis. Usually the early enlargement can be arrested by the elimination of intoxicants and correction of poor hygiene and a high carbohydrate diet with the reduction, or even elimination for a time, of red meats.

Kenneth M. Lynch, of Charleston, has just reported four primary cancers of the liver and their relation to "yellow atrophy cirrhosis." I have never seen a similar suggestion, and it deserves close attention. Three patients who were tested had positive Wassermanns, and only one showed syphilis at necropsy. His article gives a review of the literature.*

DISCUSSION (*Abstract*)

Dr. Julius Friedenwald, Baltimore, Md.—As has been pointed out, primary carcinoma of the liver is a rare affection. The incidence reported by most observers is less than 1 per cent. The high incidence observed by Strong and Pitts of 7 per cent in the autopsies in Chinese is accounted for by the frequency of a preceding chronic infection of the liver and cirrhosis.

It is generally admitted that cirrhosis usually precedes the cancerous involvement, though there have been some reports of instances in which both conditions were said to occur simultaneously or even that the cirrhosis was produced as the result of the carcinomatous invasion.

Winternitz years ago explained the relation of cirrhosis to carcinoma on the following basis. Due to injury a destruction of liver tissue occurs, on account of which fibrosis and regeneration take place. This is followed by a production of hyperplastic nodules of liver cells and bile-duct structures, ordinarily observed in cirrhosis. These formations have the appearance of true adenomata. On account of the continuance of the injury the necrosis and regeneration continue, the cells lose their function and through an excessive proliferation develop into malignant growths.

The two following instances of primary carcinoma of the liver associated with cirrhosis are of interest:

Case 1.—A woman, aged 52 years, complained of abdominal discomfort especially located in the upper right abdomen, which had been annoying her for several years, but which had gradually become more aggravated. In addition there had been pressure and distention in the lower abdomen at times with occasional nausea, acidity of the stomach, eructations, and constipation. The patient had not had any previous serious illnesses and her family history was unimportant. She had lost 10 pounds in weight.

On physical examination there was evidence of loss

*Sou. Med. Jour., **30**:1043 (Nov.) 1937.

of flesh and the sclera and skin presented a slight icterus. The abdomen was soft, extremely relaxed; the liver extended slightly below the costal arch and there was a slight degree of tenderness in this area as well as in the lower abdomen. The spleen was not palpable. The urine was normal, with the exception of a trace of bile. The non-surgical biliary drainages presented turbid bile, somewhat greenish in color, but containing large fractions of "B" bile with cholesterin crystals and mucus, and revealed in addition a definite colon infection.

The roentgen ray report was as follows: prolapsed fish-hook stomach, actively contracting and pulled over and held in the upper right quadrant; no defects; duodenal cap not deformed.

The diagnosis arrived at was cholecystitis with possible beginning cirrhosis of the liver.

Under treatment the patient improved markedly in health with relief from all abdominal distress. All evidence of the slight jaundice heretofore noted had disappeared; she made a gain of 10 pounds in weight and appeared to enjoy normal health. A year following her first visit she again returned with a history of having a drawing discomfort in the upper right quadrant of the abdomen with distention during the preceding two weeks, together with a progressively increasing jaundice. On examination, the liver was found apparently smaller than at the previous examination and a large quantity of free fluid was noted in the abdomen. The skin and sclera were deeply jaundiced.

Operation was advised. About 500 c. c. of a straw-colored fluid escaped from the abdominal cavity; the liver was found small, hard and definitely cirrhotic and contained numerous nodules.

The autopsy revealed a primary carcinoma of the liver with cirrhosis and hemorrhagic ascites.

Case 2.—A male, aged 47 years, had been addicted to the use of large quantities of alcoholic drinks extending over many years. For over a year he complained of indigestion and suffered each morning with nausea and frequently with vomiting. There was loss of appetite, abdominal distention and discomfort in the right upper quadrant of the abdomen with increasing pain in this region as well as about the right shoulder blade.

The physical examination revealed considerable general emaciation and secondary anemia, edema of the legs and abdominal distention. There was present a definite abdominal fluid wave and movable dullness. The liver was decreased in size and a rounded mass was noted in the mid epigastrium. From the history, especially of alcoholism, and the physical signs, the diagnosis of cirrhosis of the liver was made. The patient became increasingly weaker and signs of coma appeared. He died in a few days following admission.

The autopsy revealed the presence of a primary carcinoma of the liver with cirrhosis and a general arteriosclerosis.

It is of interest to note the frequent association of primary carcinoma of the liver with cirrhosis. It is probable that in most instances the cirrhosis precedes the development of the growth.

Dr. John Minor, Washington, D. C.—In opening the discussion of this interesting paper I shall focus my attention largely on the problem of cirrhosis. Dr. Rice has pointed out the frequent association of cirrhotic processes with neoplasia in the liver, an association which has long interested pathologists. The obvious suggestion is that a chronic irritation sets up a regeneration reaction which may be a direct incitant to new growth.

The enormous capacity of the liver for rapid regeneration was spoken of this morning by Dr. Mann, an authority on the subject. His work, with McGath and others, and the work of Whipple and Sperry, Fishback and others, has shown that the liver can more than replace the removed mass in from six to eight weeks, with functioning liver tissue, in the presence of a sufficiently intact portal blood supply; and Fishback has shown that the rapidity of this replacement is proportional to the injury.

How early may a reasonably sure diagnosis of cirrhosis be made? We see frequently patients with definitely enlarged livers, only a proportion of whom (subsequently) develop clinical liver disease. Many of these occur in moderate to severe alcoholics. There is no doubt that cirrhosis with considerable liver enlargement may at times go on for a good many years, with very gradual development of liver insufficiency. In the early stages liver enlargement is the rule; an alcoholic history is frequent; and a careful clinical and laboratory study may give us sufficient evidence to warrant a diagnosis and a therapeutic approach.

Laboratory data are often very uninforming. In addition to the usual hematologic and serologic study of the blood the icterus index, or the van den Bergh, some type of liver function test as the bromsulphalein or Takata-Ara or the more recently suggested hippuric acid synthesis test; a study of the blood for the suggestive presence of macrocytosis, and of the blood protein factions, may add a good deal to our knowledge of the case. It is, however, important to recognize that sound clinical study, with the addition of the simpler laboratory data which can be carried out by any of us, is usually sufficient to give us a clear lead. In other words, complicated laboratory determinations are not essential to proper handling of these cases.

If such a diagnosis is made, can anything be done about it? Evidence both experimental and clinical goes to prove that something can be done, if a consistent program (in the effectiveness of which the physician believes) can be carried out, though it requires long-term effort on the part of both physician and patient.

The evidence Dr. Mann referred to this morning points the way. High carbohydrate intake clearly accelerates liver repair, and as clearly in experimental animals protects the liver from damage provided the portal circulation be not too severely impaired. We cannot determine the degree of damage the portal circulation has suffered. It is doubtless in considerable degree proportional to the duration of the toxic or irritative process in the relatively slowly developing sclerotic processes. In acute toxic necrosis, blood supply is usually little impaired and carbohydrate in one or another form has been shown to be the only effective therapeutic measure, in acute yellow atrophy, whatever the toxic agent causing it.

I would urge you to review the very interesting work by Mann, Bollman and their associates, and the rapidly accumulating recent work by others on these phases of liver physiology and pathology. Mann's and Bollman's work with carbon tetrachloride cirrhosis is particularly suggestive.

In conclusion, I wish especially to call attention to the probability, on the grounds stated above, that cirrhosis as a clinical entity may be a reversible process, capable of clinical recovery if treated along the lines ex-

perimental pathology and physiology have pointed out. It has been shown by several workers that high grade liver toxemia from liver destruction in the course of portal cirrhosis is capable of relief; that jaundice and ascites may disappear and clinical restoration be extraordinary. I want to urge those who deal with liver disease to take a hopeful attitude and to use the weapons which lie at hand to combat conditions usually considered hopeless.

HEREDITY IN CANCER OF THE BREAST*

By MORTON J. TENDLER, M.D., F.A.C.S.
Memphis, Tennessee

The occurrence of carcinoma of the breast in three sisters, and the fact that one maternal aunt and one maternal grandaunt of the same family were known to have succumbed to the same affliction, would seem further to substantiate one of the older theories of carcinogenesis. That the unmarried sister was several years older than the two who were married, and the affected members of previous generations were of the maternal line, are observations consistent with the newer theories of factors which enter into the development of mammary cancer.

CASE REPORTS

Case 1.—Mrs. F. G. W., aged 42 years, housewife, nullipara, was first seen on August 15, 1929. Her past history revealed nothing of consequence. Her chief complaint was pain and soreness in the right breast. The symptoms had begun four months previously with a sensation of needles pricking deeply in the breast. This was followed two months later by pain and swelling in the upper outer quadrant, the pain radiating to the shoulder, upper arm, and side of the neck on the right. The following month the pain and swelling extended throughout the breast, and an ulcer appeared and increased in size. There had been some oozing from the ulcer, but no bleeding from the nipple.

From her general appearance, the patient seemed in excellent health. Routine laboratory studies were negative and the physical examination, except for the breasts, showed nothing unusual.

In the central portion of the left breast was an indefinite, lobulated mass, freely movable, semi-hard, and painless. It measured 8 cm. in diameter and approximately 4 cm. in depth in the thickest portion. The patient stated that this mass had been present for at least ten years, had not grown nor changed during that time, and had never caused her any distress.

The right breast was approximately one and one-half times as large as the left and 2 cm. higher on the thorax. Two definite rounded masses could be distinguished. The larger, 10 cm. in diameter, was in the upper and outer quadrant; it was hard, irregular in outline, and fixed to the skin and the thoracic wall. The skin over this portion was perceptibly raised, of the typical orange peel pattern, and reddish blue in color. In the center of the cyanotic area was a shallow, irregular ulcer 2 cm. in diameter, its base covered with grayish granulation tissue. The lower mass, situated in the lower outer quadrant, was only slightly smaller than the upper. There were no apparent changes in the skin, but the nipple was retracted. Movement of the right shoulder and upper arm was decidedly limited, but no glands nor masses could be palpated in the axillary or clavicular areas.

The diagnosis was cystic disease of the left breast and inoperable medullary carcinoma of the right breast. Following deep roentgen ray therapy, the tumor masses on the right shrank perceptibly, the ulcer healed, and the entire breast became freely movable. A radical amputation, by the Stiles technic, was performed on September 29, 1929, and, at the patient's request, a simple mammectomy was done on the left two weeks later. Recovery from both operations was uneventful. The pathologist's diagnosis on the specimen from the right was scirrhous carcinoma of the breast with axillary metastases (*Figs. 1* and *2*).

The patient subsequently received a course of deep x-ray therapy, but died in December, 1931, from metastases in the liver and both lungs.

*Case 2.**—Mrs. M. G. McD., aged 48 years, housewife,

*Read in Section on Surgery, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

*For this report the author is indebted to the patient's daughter, Mrs. V. McD. H., her sister, Miss M. G., and her physicians in Junction City and Shreveport.

Fig. 1, Case 1
Microscopic section revealing typical scirrhous carcinoma of breast. See text for description.

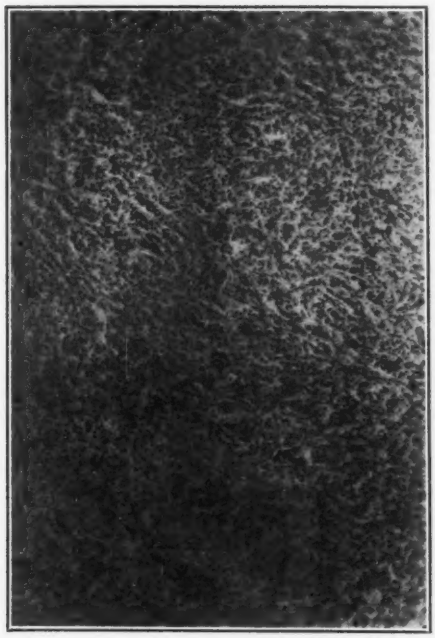

Fig. 2, Case 1
Microscopic section revealing carcinomatous axillary lymph node removed at operation with breast. See text for description.

para 1, whose home was in Junction City, Arkansas, consulted Dr. P. H. Muse, of that city, in September, 1934, in regard to a lump which had been present in her left breast for two years. Dr. Muse's clinical diagnosis was inoperable carcinoma of the breast. She was referred to Dr. H. G. F. Edwards, of Shreveport, Louisiana, who confirmed the clinical diagnosis by biopsy and the finding of a scirrhous carcinoma. Dr. Edwards' gross report was as follows:

"The entire left breast is infiltrated with a hard, uniform tumor mass. The skin has a peau d'orange appearance. There is retraction of the nipple. The lower outer quadrant reveals areas of marked skin infiltration almost breaking through. The breast is fixed to the chest wall. There is a large axillary node definitely fixed."

Microscopy revealed a scirrhous carcinoma of the breast.

The patient was given deep x ray therapy over the breast, as well as radium implantation. Although the local lesion was held in abeyance and rapidly resolved, she died on May 22, 1935, of metastases to the chest and to the long bones. She sustained a pathologic fracture of the left humerus shortly before death.

Case 3.—Miss M. G., aged 60 years, a retired school teacher, was first seen on November 7, 1934. Her personal history was unimportant. Three months earlier she had noticed a swelling in the inner lower quadrant of the right breast; there had been no inflammation, bleeding of the nipple, nor areolar irritation. She had been advised by a chiropractor, whom she had consulted for another condition, to see a surgeon in regard to the lump, but had not done so until she learned that her second sister had cancer of the breast.

The patient's appearance was normal, her general physical examination negative, and the laboratory findings were insignificant.

The left breast was pendulous and thin, and hung 1 cm. lower than the right. The right breast was no larger than the left, but its nipple was inverted and in its inner quadrant, 5 cm. from the nipple, was a definite depression or dimple. There was no ulcer nor discharge. Beneath the dimple a mass the size of a large English walnut could be palpated. This was hard, irregular in outline, not tender, and freely movable upon the underlying musculature, but attached to the overlying skin. The appearance of the skin was normal. In the right axilla anteriorly was a subpectoral mass 1 cm. across, movable and not tender. No other axillary masses were detected.

The diagnosis was early carcinoma of the breast. The patient received deep x-ray therapy preparatory to operation, and a radical amputation was performed on December 2, 1934. The pathologist's diagnosis was adenocarcinoma of the breast, with no gross evidence of metastatic involvement of the axillary nodes (*Fig. 3*).

The patient received two courses of roentgen ray treatments following operation and has continued to present herself for examination at intervals of every few months. Three years have passed since the operation

Fig. 3, Case 3
Microscopic section revealing adenocarcinoma of breast. See text for description.

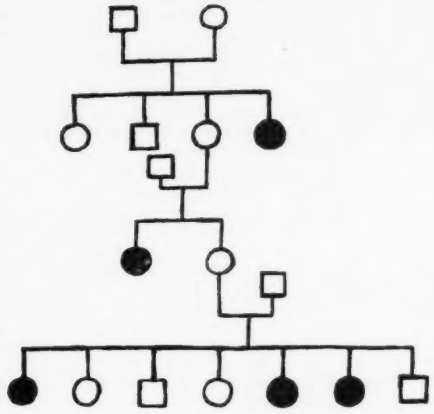

Fig. 4

Family chart of the cases herein reported, showing carcinoma of the breast in the maternal grandaunt and aunt, and three sisters.

and her health has remained good to the present time (*Fig. 4*). (Slides of sections and family tree.)

For more than a century, recorded histories of families in which several members were afflicted with cancer, often of a single type and identical in location, have inspired interest in the inheritability of cancer. Within the past thirty years an ever increasing amount of research has been carried out in this field. Comparative observations on cancer in human families and in selected strains of mice have revealed a similarity of developmental factors sufficiently close to warrant an analogy between the two species in these respects.

A host of indefatigable workers have contributed to our present knowledge of the genetics of cancer. Studious observers of human families have been Bauer, Ewing, Little, Paulsen, Warthin, Wells, Williams, Wolff, and others. The opinions of a few of these might well be given.

Warthin,[36] after exhaustive clinical, pathological and statistical studies, concluded:

"The definite and marked susceptibility to carcinoma exists in certain families and family generations. This family tendency is usually most pronounced when there is a history of cancer in both paternal and maternal lines. In such families, there is an especial tendency for carcinoma to appear at an earlier age than in the forbears, and in these younger individuals the cancer usually shows an increased malignancy."

Ewing[10] states:

"All the evidence available points to an organ specificity in any hereditary factor which may exist. General pathology abounds in data regarding the occurrence of cancer in different types of organ and body conformation. * * * It is to be noted that in these instances the hereditary factor relates to organic peculiarities, and has nothing to do with the effective exciting factors in cancer. Clinical study of heredity in cancer might well direct its efforts toward establishing the importance of these and other organic characters, undoubtedly inherited, rather than toward the effort to maintain or disprove the existence of a universal tendency to cancer."

Wells[38] thinks that it seems safe to maintain that the existence of an hereditary influence on the susceptibility and resistance to cancer has been established for both animals and man.

From an analysis of family histories at the Eugenics Record Office of the Carnegie Institute at Washington, Little[19] showed that the progeny of a cancerous mother and non-cancerous father were found to contain an excess of cancer, and regarded this fact as conclusive evidence of an hereditary tendency in the growth of cancer in mankind.

Among those who have devoted their attention to animal experiments in cancer inheritance are Bagg, Bittner, Cori, Fekete, Gardner, Green, Lacassagne, Lathrop, Little, Loeb, Lynch, J. A. Murray, W. S. Murray, Slye and Strong.

The weight of opinion from all these studies seems to be that an inherent constitutional susceptibility is the prime factor in cancer development in both human beings and animals, and that superimposed upon this general tendency there must be an inherited local or organic susceptibility to the disease. This view supports the theory, advanced long ago by Cohnheim, that congenital abnormalities in cytoplasm determine the site of cancer, and explains also the tendency of the growth to appear in a specific location in several members of one family. These congenital tendencies may be so strong as in themselves to be responsible for the development of cancer in a few cases, especially for those of a high degree of malignancy which appear in individuals at an early age. In others of the same family and generation, however, who constitute the large majority, cancer develops at middle age or late in life, or perhaps not at all, indicating that the genetic factor is less pronounced or latent, and must be acted upon for varying periods of time by other agents, exogenous or endogenous. It is the explanation of this fact which Warthin[37] considered the chief genetic problem of today.

The present status of our knowledge of inheritance of the majority of cancers has been well stated by Slye:[32]

"The inheritance of cancer susceptibility alone is probably not always sufficient to insure the occurrence

of malignancy. An external factor acting with internal factors on a susceptible soil is probably the cause of cancer. The interrelation of these provocative factors may be very complicated and, in addition, the occurrence of cancer in a family may be greatly modified by other metabolic conditions. The longer the life span of the individual, the greater the probability the provocative factors will arise in their necessary interrelationships."

Slye's statement relates particularly to those tumors influenced by exogenous factors, as infection, radiation, and extraneous chemical substances, whose role in cancer development is fairly well understood. In certain organs, however, tumor growth is believed to be affected by internal secretions and metabolic disturbances, quite unassociated with external factors. Although the part played by these internal agents is not wholly clear, recent intensive investigations have justified some definite conclusions regarding their activity, especially as to the influence of the estrogenic hormones in the production of carcinoma of the breast.

Early studies in this field were carried out by Lathrop and Loeb,[17 18] Loeb,[22 23 24] and Cori,[9] who demonstrated the relationship between the action of ovarian secretion and mammary cancer. By ovariectomizing mice at different ages, they found (1) castration served to reduce the incidence of mammary tumors in female mice of a highly susceptible strain; (2) the earlier the age of the animal at castration, the lower the tumor incidence and the later tumor appears; (3) the effect of castration is not equally pronounced in all strains; (4) the cancer incidence is lower and tumor age higher in mice that are prevented from breeding than in breeding animals; (5) the incidence of tumors among nonbreeding as well as breeding mice is different for each strain; (6) although the tendency to inheritance may be present from both the father and mother strain, the tendency in the mother strain dominates in cancer development (which agrees with Little's findings from investigations in human families, mentioned above); (7) there exists a relation between the tumor age and tumor rate in breeding mice: the lower the tumor incidence the older the mice when tumors appear; and (8) after a certain quantity of hormone had acted, the cancerous transformation would occur subsequently, even though the action of the hormone had ceased some time before the first appearance of cancer (thus explaining the development of cancer after the menopause).

Murray and Little, Slye, Bittner, Strong, and a number of others have conducted similar experiments, with concordant findings. There is, however, some differences of opinion as to the manner in which these conditions take place. Murray, Little and others believe that mammary cancer does not follow the Mendelian law of inheritance, and that the tendency is derived from extrachromosomal influences. Another school takes opposite views. These differences have not altered the conception of the question as a whole.

At first it was believed that mammary cancer was sex limited, but this theory was disproved by Murray[28] in 1928. By transplanting whole ovaries into the abdomen of castrated male mice, he produced mammary cancer in 7.1 per cent of the animals.

The isolation of estrin by Allen and Doisy,[3] and the discovery by Kennaway[15] and his collaborators of a common molecular structure in estrin and certain chemical compounds, known as the phenanthrene ring, led to experiments upon male as well as female mice with both estrin and a number of these chemical substances. The results have borne out the findings from studies of the effects of castration.

In general agreement with the results of other investigators were those of experiments carried out by Suntzeff and Loeb[35] and their co-workers, and by Lacassagne,[16] and we may therefore accept their opinions as representative. Employing opposite methods of study, these two reached identical conclusions.

By increasing or decreasing the amount of hormone injected into a given family or strain, Loeb *et alii* have shown that the development of spontaneous mammary carcinoma in mice is due to ovarian hormones acting upon mammary tissue which is made especially responsive to such stimulation by hereditary factors, and that the greater the amount of hormone which is allowed to act, the greater the effect. Further, the fact that the tumor age is relatively low in strains with a high incidence is interpreted as indicating an intensity factor influencing both the cancer rate and cancer age: the stronger the factor, the higher the tumor rate and the lower the tumor age. This intensity factor consists in the hereditarily determined responsiveness of the mammary gland to stimulation by ovarian hormones.

By the reverse process of giving an equal amount of hormone to animals of different strains, Lacassagne has shown that the hereditary factor seems to consist in an unequal response of the same organ in different strains

to the same quantity of hormone. He found this apparent not only from the varying tumor incidence and ages of the animals, but also from the strikingly different histological structures of the breasts in different strains following the same treatment.

Little[21] sums up his own results, which are in accord with those of Loeb and Lacassagne, as follows:

"The technic of keeping the genetic constitution constant and varying the ovarian and mammary functions has given sufficient information to make it possible to recognize that the degree and extent of those functions is a factor of the internal environment of the individual which may importantly affect the incidence of breast cancer.

"The technic of keeping the ovarian and mammary function constant and varying the genetic factors has shown that hereditary transmission of constitutional influences plays a basic role in the incidence of cancer of the breast."

It is noteworthy that these investigators confirmed Murray's finding that the mammary gland of male mice is at least as predisposed to the development of carcinoma as the female gland.

Loeb and his associates believe that the lutein hormone also aids in the production of mammary cancer and suggest that, in addition, certain hormones of the anterior pituitary gland may come into action in the breeding mice.

Approaching the question from another angle, Adair[1] observed that in 200 cases of mammary cancer in women, in only 8.5 per cent was there a normal nursing history, whereas 80 per cent of women of a control group gave a normal nursing history. Adair and Bagg,[2] and Bagg[4 5] were able to increase the incidence of breast cancer in mice from 5 to 87 per cent by artificial stagnation, and to produce a like effect by breeding and prevention of nursing. Fekete and Green,[11] after blockage of the nipples of mice, concluded that milk stagnation was influential in determining the site and time at which mammary tumors appeared in a genetically susceptible strain. From these findings, both groups deduced that the chemical irritation of retained mammary gland secretions bears a causative relation to the onset of mammary carcinoma.

It is significant, however, that none of these experimentors were able to provoke cancer by any of the methods tried in animals of strains entirely free of malignancies of the breast.

Lacassagne suggests that tumor growth may be brought about by direct carcinogenic action of estrin in certain conditions, or by retention of estrin, which, upon becoming stagnant, is transformed into a carcinogenic agent. He also states that familial differences in the reaction of organs might be due to an unequal elimination of the hormone injected.

"One may imagine that the strains slightly susceptible to cancer comprise those mice whose excretory functions rapidly promote an elimination of estrone, while in those mice susceptible to cancer, estrone may be retained, accumulating at certain points in the organism, particularly in the mammary ducts. Or, a chemical reaction might effect a transformation in the organism of the susceptible strain (but not in the resistant strain), transforming stable estrone into a more labile substance."

He points out that Zondek has shown that folliculin is rapidly destroyed, probably in the liver, while the benzoate of folliculin is not destroyed.

The substance of present information regarding the action of estrogenic hormone in mammary cancer is that they provoke cellular proliferation in the epithelial tissues and, if retained, exercise this proliferative action over a sufficient length of time to cause irritation and induce cancer.

Thus, while it has not yet been determined what lies behind the individual variations in potentiality of cancer tendency, which Warthin regarded as the important genetic problem, in mammary cancer at least, some light has been thrown upon the subject. And by this light it may be that the way will become clear to a method of prevention of cancer of the breast for those persons in whose family there is a known tendency to its inheritance.

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DISCUSSION (*Abstract*)

Dr. Geo. W. Wright, Monroe, La.—Cancer is a very complex problem. That heredity plays a role in its etiology, both in human beings and animals, is an accepted fact by many investigators and students; that with heredity furnishing a fertile field, certain inciting factors seem to be potent in the production of mammary cancer in mice is also a fact.

Many investigators have reported their findings in humans and while most agree as to the importance of hereditary factors, most reports are conflicting, principally because of the inadequacy of the methods used and the complexity of the problem. Montynova, working in the Medico-Genetical Institute in Moscow, has recently published an excellent article dealing with the pedigrees of 201 subjects. He concludes that heredity does play a definite role in the predisposition to cancer of the breast and that this predisposition is in some way concerned with a predisposition to cancer in general.

Any discussion of a paper of this title is incomplete without especial reference to the brilliant experiments of Lacassagne, alluded to by Dr. Tendler and referred to by the past president of the American Surgical Association as among the most dramatic discoveries of medicine that have been made in all time. Prefacing his excellent paper on the hormonal pathogenesis of breast cancer, he says that the essential characteristic of the cancer cell is its "loss of subordination to the rhythm of division," its endless and inexhaustible faculty of multiplication which is retained by subsequent cell generations, and its resistance to any measure which might tend to subordinate this cellular dyscrasia to the laws governing the organism. Using a normal ovarian hormone, estrone, which is known to influence cell multiplication, he was able to bring about, by continuous stimulation of the breast epithelium with massive weekly injections, a cellular disturbance resulting in cancer. In certain strains of mice which show a high female incidence of mammary cancer he was able to produce a proliferation in the male equal to that in the female, creating an equal incidence in both sexes.

Using a strain of mice of low cancer incidence, Lacassagne found that these animals were rather dilatory in their response to the hormones, but that by continued stimulation beyond an age when all the high incidence mice had died he was able to kill out all of this strain. These last tests were done in a futile effort to eliminate the hereditary factor. He concludes that two factors operate to produce breast cancer, namely, hereditary and hormonal factors.

This startling discovery is indeed epoch-making. The mere fact that cancer of the breast can be produced with equal frequency in the male and female under proper stimulation using a normal ovarian hormone is within itself a discovery of prime importance, but when one sees the practical application of these findings in the human subject in that it is perfectly possible now to take a thoroughly inoperable, bedridden case of carcinoma of the breast with widespread metastasis in other organs and apply x-ray or radium simply to bring about a recession of the normal ovarian hormone output and in the course of several months see a marked regression of the tumor masses and a patient who is able to be up and about and attend her household duties, the real magnitude of this discovery becomes apparent. I am quite sure that many of you present in this audience have seen striking confirmations of this fact.

Dr. James T. Nix, New Orleans, La.—Dr. Tendler very properly has refrained from placing any definite interpretation on his cases. Knowing the complexity of the problem of inheritance, we must proceed with great caution. Cancer is not a somatic character, like the color of the eyes, or a constitutional deficiency, like hemophilia; therefore, direct transmission from one generation to the other cannot occur. The point to be determined is whether or not susceptibility or resistance to cancer are constituent factors of the human germ

plasm. These factors are so intangible as almost to defy recognition, especially in an animal whose generations succeed each other at intervals of twenty to thirty years.

Dr. Tendler has presented a group of three sisters with carcinoma of the breast, whose maternal aunt and grandaunt had died of the same affliction. The only parallel group we recall was that observed by Sibley: a mother and five daughters who died of cancer of the left breast, as reported by Williams in 1894. The predominance of the maternal influence has been found by Murray and Little in carcimona of the breast in mice, which has led them to postulate an extrachromosomal hereditary mechanism. The same relationship has been noted in the inheritance of mouse leukemia and longevity seems to be affected in the same way. This maternal influence is obvious in Dr. Tendler's cases, yet at the Tumor Clinic of Charity Hospital of New Orleans we have seen, over a period of four years, one hundred and seventeen cases of cancer of the breast, only one of which gave a history of carcinoma of the breast in the mother. Only four other cases had a family history of cancer: in one case the only sister had cancer of the uterus and an uncle had skin cancer; in another, the mother had a malignant tumor of the abdomen; in a third, a sister died of cancer of the face; and in the last, the father had had cancer of the skin. In other words, ours has been the experience of large clinics, where, according to Guleke, the possible hereditary cases amount to about 2.36 per cent. Nothing is more attractive than Maud Slye's statement that, "It is wholly possible to eliminate cancer susceptibility from any species in two generations by the appropriate genetic procedure." Unfortunately, it seems that cancer of the breast in man does not follow such a hereditary pattern.

Dr. Tendler's cases show low reproductivity: one of the sisters was unmarried, another had no children, and the third had only one child. We can conjecture that this presented an opportunity for abnormal endocrine interplay. Lacassagne has shown that for mammary tumors, sensitivity to the proliferative action of estrone was the inherited character.

A third interpretation is made possible by the existence of definite disease of the breast in one of Dr. Tendler's cases. This, in a certain proportion of instances, has been shown to be a precursor of carcinoma.

In concluding, I should like to say that at the present time the preponderance of evidence is against the inheritance of cancer of the breast. The fact that heredity is clearly evident in such tumors as gliomas, neurofibromatosis, multiple enchondromas, indicates that were it operative for the other forms of cancer, it would have become definite by now.

Dr. Tendler (closing)—In answer to Dr. Nix's suggestion that I include in my bibliography Sibley's report in the *Medico-Chirugical Transactions* of 1859 concerning the family in which the mother and five daughters had cancer of the breast, I might mention that in a previous article I did include it in my bibliography, but was forced to exclude it in this latter one because of the fact that the history and description of the specimens of these cases were a little too vague for finality.

I am sure that most of us are open minded on the subject of heredity, and the resulting comparisons between man and other biologic groups, yet I think H. Gideon Wells struck an interesting note in discussing Maud Slye's work, when he made this statement:

"The laws of heredity are fundamental by-laws, applicable to every living thing, whether plant or animal. Mendel worked out the plan of heredity with garden peas, and these have been found to hold good for all multicellular living things, whether plants or animals, peas or mice, insects or cows. If the laws of heredity established with peas hold good for mice, they should for men, for there is far less difference between mice and men than mice and peas."

I am very much interested in these slides which I now show you. These are two photographs taken of a fourth sister of this family, who was treated by a so-called cancer specialist in Texas, showing what sort of treatment he is employing in cancer of the breast. This sister, living in Oklahoma City, was first seen by Dr. R. M. Howard, Professor of Surgery at the University of Oklahoma. In a personal communication he told me that there was a suspicious lump in the right breast with no fixation to the skin or nipple and no palpable glands in the axilla nor in the clavicular region. He could not say definitely what type of process was present. He suggested immediate biopsy in order to determine the type of lesion. The patient went home; discussed the matter with her husband, and in a few days they were on their way to Texas to obtain a non-surgical cure for cancer. And mind you, no biopsy had been taken nor was it ever taken before treatment was begun on this patient. You see a complete destruction of the breast by some sort of escharotic agent and in the next photograph you see the horrible scar left by this terrible procedure. I shall be very much interested in following this case to its termination; first, to determine whether the tumor, apparently quite small, was completely eradicated by this method, and secondly, if it was cancer, whether this type of procedure, entirely local in its treatment, is sufficient to cure even a grade 1 carcinoma.

In a personal communication, Dr. Hugh Trout of Roanoke, Virginia, suggested that we should not neglect the work being done by Dr. Clara Lynch on cancer in twins.

PLACENTA ACCRETA*

By Arthur Charles Tiemeyer
B.S., M.D., F.A.C.S.
Baltimore, Maryland

Placenta accreta is a rare anomaly in which there is an absence in whole or in part of the decidua basalis, with the implantation of the placenta directly upon or into the uterine muscularis. There is no spongy layer of the decidua basalis; hence there can be no line of cleavage between the placenta and the uterine wall. Therefore, normal separation in the third stage of labor is impossible. When the entire maternal surface of the placenta is attached to the uterine

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wall, the condition is known as a complete placenta accreta, but when only portions are so attached and there are areas of normal decidua basalis, it is called a partial placenta accreta. When the villi invade the musculature and become firmly incorporated with it, the condition is called placenta increta.

Two cases will be presented. The first one was reported[1] in 1931. Both are of the complete variety and are from my service at the West Baltimore General Hospital. The two cases occurred in 4,312 deliveries, or an instance of 1 in 2,156 cases. Irving and Hertig,[2] of the Boston Lying-In Hospital, report their instance as 1 in 1,956 deliveries. The reported frequency of this rare anomaly varies in the literature from 1 in 1,956 deliveries to as infrequent as 1 in 40,000 deliveries. About 100 cases have been reported. The cases should be classified as an accreta only when thorough microscopic study shows an absence of the decidua basalis or in those cases where most of it is missing, particularly the spongy layer. One not infrequently finds small areas in a normal implantation where an individual cotyledon is directly attached to the muscularis.

REPORT OF CASES

Case 1.—Mrs. M. P., white, aged 33 years, has had 8 children, and was admitted to the hospital on June 28, 1930, with a diagnosis of retained placenta. Six hours before admission she was delivered at home by her family physician, the first two stages of labor lasting 40 minutes. Delivery was spontaneous. The baby was a female at term and weighed 3,048 grams. After two hours of third stage of labor, there was no placental separation and no abnormal bleeding. Several unsuccessful attempts were made to express the placenta by Credé's maneuver and then manual removal was tried. Several pieces of placental tissue were torn away and the patient began to bleed. The uterus was packed and she was sent into the hospital, where I first saw her. Here another attempt was made to express the placenta, and when this failed the patient was anesthetized and the hand was introduced into the uterus, but no line of cleavage could be found. A tentative diagnosis of placenta accreta was made. Because of bleeding and shock, the uterus was again packed and the patient was given a transfusion of 600 c. c. of blood. She was permitted to recover from the shock. During the intrauterine manipulation the wall of the uterus at the fundus was found to be so thin that intestinal peristalsis could easily be felt through the uterine wall. On the following morning she was again transfused and a supravaginal hysterectomy was done. The patient made a good recovery, although there was some superficial wound infection and she was discharged from the hospital on the twenty-seventh day after operation.

Pathologic report by Dr. Manual Gichner follows: Grossly the specimen consisted of a postpartum uterus removed supravaginally and contained a large portion of the placenta densely adherent to the uterine wall, particularly at the fundus, where it seemed to invade the muscularis.

Microscopically, sections prepared included the uterine wall and the adherent placenta. No evidence of decidua basalis was seen and in several areas, notably at the fundus, the chorionic villi invaded the underlying musculature and formed interdigitations with strands of muscle.

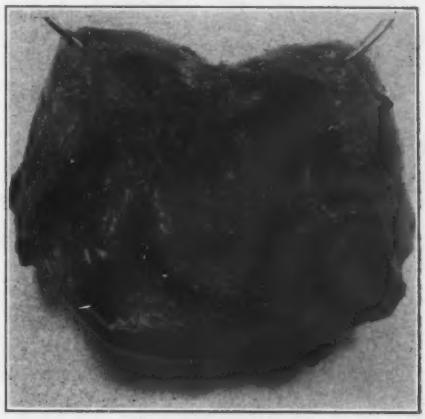

Fig. 1, Case 1

Untouched photograph showing opened uterus with placenta attached. Note invasion of myometrium and thinning of uterine wall at the fundus.

Fig. 2, Case 1

Photomicrograph (x 42). Myometrium very thin and invaded by villi almost to the peritoneum. The increased vascularity of the uterine wall is apparent, although many of the vessels are sclerosed. Decidua basalis is absent.

Fig. 3, Case 1
Photomicrograph (x 42). Invasion of myometrium by chorionic villa. Decidua basalis is absent.

About these areas of invasion there was marked increase in circulation and considerable free blood in the tissues.

The diagnosis was complete placenta accreta.

The important points in the history were as follows: there were 8 pregnancies in 14 years, all normal, except the seventh and the present one. The seventh pregnancy terminated from some undetermined cause at the twenty-eighth week and was complicated by retained placenta requiring manual removal, and puerperal sepsis. On the tenth day postpartum, because of hemorrhage from the uterus, the patient was removed to a hospital for a curettement, and portions of retained placenta were removed. Her convalescence was marked by 27 days of fever and she remained in the hospital for 36 days after curettement. She presented no evidence of ovarian dysfunction.

Case 2.—Mrs. M. R., white, aged 20 years, first pregnancy, was admitted to the hospital from the prenatal clinic in active labor on July 17, 1936. She was 30 weeks pregnant, and her membranes had ruptured during sexual intercourse on the night before admission. There was nothing abnormal in her history except scanty menstruation. Her periods began at the age of 14 years, were regular every 28 days and lasted from two to three days. In the 16 months immediately prior to her pregnancy the menstrual periods gradually diminished in amount and lasted only one or two days, sometimes there was nothing more than a spotting. The patient had received some form of hormone therapy and was told that this was to stimulate her ovaries. She had no dysmenorrhea. She was married for three years, used no contraceptives and was examined for sterility a year before becoming pregnant. She had had no intra-uterine instrumentation done nor was there a tubal patency test made. She was told that her uterus was smaller than normal.

Twelve hours after rupture of the membranes, labor started. The first stage lasted 14 hours, the second stage an hour and ended with the spontaneous delivery of a living female infant weighing 1,304 grams. After a third stage of labor lasting two hours and during which time there was no abnormal bleeding, Credé's maneuver was tried, but the placenta could not be expressed. Manual removal of the placenta was tried, but this likewise was unsuccessful. The resident physician could find no line of cleavage, so further attempts to remove the placenta were abandoned. The intra-uterine manipulations started a moderate amount of uterine bleeding. I advised packing the uterus and matching the patient's blood for a transfusion. Six hours later

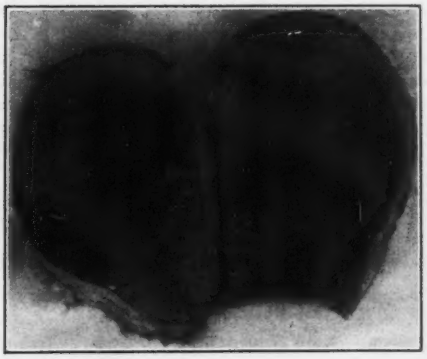

Fig. 4, Case 2
Uterus opened showing attachment of placenta to fundus and body, with extreme thinning of wall of the body of the uterus.

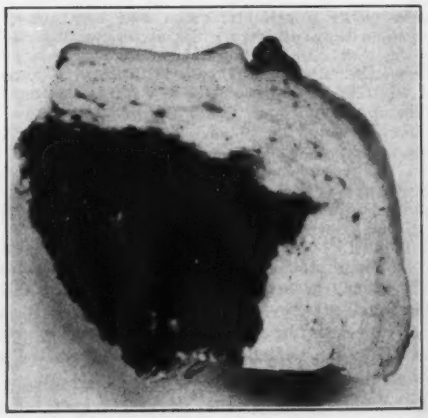

Fig. 5, Case 2
Section of wall of uterus showing firm attachment of placenta and invasion of myometrium by placental tissue.

she was taken to the operating room, which had been prepared for laparotomy. The packing was removed from the uterus and its interior was explored. No line of cleavage could be found. The patient was immediately transfused and a supravaginal hysterectomy was done. The abdomen was closed without drainage. On the third postoperative day there was a rise of temperature to 102.4° F. by mouth, and she developed a pneumonia, from which she recovered. She was discharged from the hospital 31 days after operation.

Pathologic report by Dr. Ralph Mostwill, pathologist of the hospital, follows: Grossly the specimen is that of a postpartum uterus which has been opened in the midline of the anterior wall. The placenta fills the interior of the uterus and is firmly attached at the fundus and body. The body of the uterus is very thin.

Numerous sections for microscopic examination were taken from the uterine wall and the placenta and several sections were taken from the decidua vera. The muscularis shows marked evidence of bleeding into the tissues. In many areas chorionic villi were growing down into the uterine wall. Myometrial tissue was drawn up into the placental septa. Only rarely does one see any evidence of decidua. At no place could a spongy or a definite compact layer of decidua be found. Excessive vascularity of the myometrium beneath the placenta was noted in many areas. Rohr's fibrin layer was imperfectly developed and could occasionally be seen at the junction of the villi with the myometrium. The decidua vera was notably free of glandular structures and was considerably thinner than normal. The spongiosa was poorly developed in the decidua vera.

The diagnosis was complete placenta accreta.

The important points in this case were the

Fig. 6, Case 2
Photomicrograph (x 42). Myometrium drawn up into placental septum, direct contact of villi with myometrium and absence of decidua basalis.

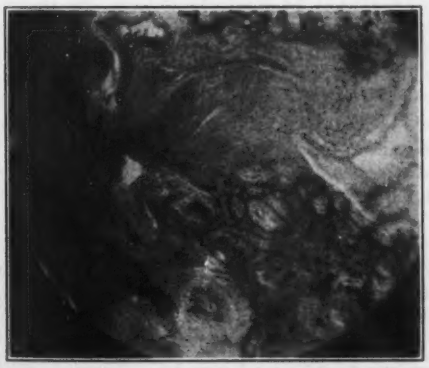

Fig. 7, Case 2
Photomicrograph (x 42). Marked invasion of myometrium by chorionic villi. No evidence of any decidua.

Fig. 8, Case 2
Photomicrograph (x 42). Direct implantation of placenta upon myometrium, dilated vascular spaces, mild inflammatory reaction.

Fig. 9, Case 2
Photomicrograph (x 42). Direct implantation of placenta upon myometrium, no decidua, indistinct Rohr's fibrin stria fused with the myometrium.

history of sterility, a single pregnancy, probably an ovarian deficiency with an underdeveloped uterus but no history of endometrial infection or instrumentation. Her basal metabolic rate was minus 10.

No attempt will be made to review the literature because two very excellent papers with complete reviews have recently been published, one by Phaneuf[3] in 1933 and the other by Irving and Hertig[2] in 1937.

ETIOLOGY

No definite cause is known, although placenta accreta occurs much more frequently in multipara than in primipara; it is much more common in women in the third decade of life and particularly in women who have had numerous pregnancies, often with a history of previous manual removal of the placenta, sepsis and curettement. We are certain that a normal endometrium is necessary for the development of a normal decidua. Therefore anything that changes the normal histological structure of the endometrium may be at least a contributory cause. We are also certain that the hormone, progesterone, promotes the development of the deciduae, and as I noted in a previous paper,[1] abnormalities of the corpus luteum may have an important bearing upon the formation of this anomaly by causing a defective decidua. The fault may be within the ovum itself in which the erosive power of the trophoblast may be excessively stimulated and the villi destroy the decidua basalis and bury their way into the muscularis. Kwartin and Adler[4] called attention to the possibility of insufficient antiferment production against the erosive action of the trophoblast. However, neither of these theories would explain why a deficiency in the decidua vera was so frequently found.

In the first case of this series rapidly repeated pregnancies, previous manual removal of the placenta and sepsis seem to play an important role in the etiology. In the second case, the woman was a primipara, and placenta accreta is a rarity in women who have not previously borne children. In this case there was a history of sterility, underdevelopment of the uterus and a deficient ovarian function. Possibly these conditions may have been the determining factors in causing placenta accreta.

Diagnosis.—Naturally a diagnosis cannot be made until the lack of placental separation in the third stage of labor. Several cases have been observed at the time of cesarean section for placenta previa. Because there is no line of cleavage there can be no normal separation of the placenta. A well developed spongy layer of the decidua is necessary for normal placental separation. In the absence of placental separation there will be very little bleeding until after attempts have been made to remove the placenta. This is quite contrary to that found in cases of retained placenta due to hourglass contraction of the uterus. This is well worth remembering. When the interior of the uterus is explored in placenta accreta, no line of cleavage can be found, while in the case of a simple retained placenta the line of cleavage can readily be found and the placenta separated from the uterus without difficulty.

Treatment.—Once a diagnosis of placenta accreta has been made, supravaginal hysterectomy offers the patient the best chance of recovery. While this may seem radical, yet when the impossibility of removing the placenta satisfactorily by any other means is considered, and also the possibility of rupturing the uterus, the high percentage of sepsis and fatal hemorrhage, this treatment becomes the most conservative.

In the literature, those cases treated by manual removal or by curettage, the mortality was about 65 per cent; those cases treated by partial manual removal and vaginal hysterectomy had a mortality of approximately 36 per cent, those cases treated by partial manual extraction and supravaginal hysterectomy had a mortality of 20 per cent; those cases treated by supravaginal hysterectomy with no attempt at manual removal had no mortality, while those cases in which the placenta was not removed at all showed a mortality of 66 per cent.

Before resorting to hysterectomy, however, the interior of the uterus should be explored. If no line of cleavage can be found, no further attempt should be made to deliver the placenta, and under no circumstances should pieces of placenta be torn away. This will invariably cause hemorrhage and the uterus may be perforated. Never curet the uterus. Do not operate while the patient is in shock. Transfuse her, pack the uterus to control hemorrhage and when the patient has reacted satisfactorily, do a supravaginal hysterectomy.

SUMMARY AND CONCLUSIONS

(1) Two cases of complete placenta accreta are presented. The instance in this clinic is 1 in 2,156 deliveries.

(2) In both cases there was an absence of decidua basalis with marked thinning of the uterine wall. In the second case there was also a defective decidua vera.

(3) In the first case, rapidly repeated pregnancies with a history of previous manual removal of the placenta, sepsis and curettement of the uterus were possible etiologic factors.

(4) In the second place, ovarian hypofunction and underdevelopment of the uterus were possible causes.

(5) A hormone theory is discussed.

(6) There was no abnormal bleeding from the uterus until after attempts were made to deliver the placenta.

(7) The diagnosis can be made by finding no line of cleavage between the placenta and the uterus.

(8) Manual removal of the placenta should not be attempted, nor should pieces of placenta be torn away from the uterine wall. Never curet the uterus in placenta accreta.

(9) Supravaginal hysterectomy is the recommended treatment.

(10) More frequent use of transfusion is recommended.

(11) Shock should be treated before the patient is subjected to abdominal surgery and bleeding controlled by the use of uterine packs while preparing for laparotomy.

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101 West Monument Street

BONY INTRACRANIAL TUMORS*

WITH REPORTS OF THREE CASES

By COBB PILCHER, M.D.
Nashville, Tennessee

Intracranial osteomas may arise in the frontal or ethmoidal sinuses or from other portions of the skull. Furthermore, as will be pointed out, bony growths may occur intradurally. Although they are relatively rare lesions, the occurrence of these osteomas has been recognized since the first description by Home[1] in 1791. In 1851, Sir James Paget[2] gave a description of these tumors upon which little or no improvement can be made today:

"Their nodular form and uniform hard, ivory-like texture; their growth in the diploë or sinuses as isolated or narrowly attached masses; their tendency to extend in all directions; their raising and penetrating the bones of the skull, and growing into the cavities of the skull and orbit, all show the exceeding difficulty and perils of operations on them."

OSTEOMA OF THE FRONTAL AND ETHMOID SINUSES

Giving support to Paget's pessimistic attitude, the only cures of sinus osteomas reported prior to 1871 were those of Lucas[3] and Hilton,[4] in each of which the tumor, after invading the orbit and destroying the eye, fell out spontaneously. (A similar spontaneous cure was reported by Bland-Sutton[5] in 1922.) Dolbeau,[6] in 1871, reported the first successful removal of an orbital osteoma, followed, in 1881, by Knapp,[7] and in 1887 by Andrews[8] (two cases). In 1898 Tauber[9] found in the literature twenty operated cases with nine deaths. By 1935, Carmody[10] tabulated only 139 osteomas of all accessory sinuses, but Gatewood and Settel[11] found 147 of the frontal sinus alone.

Meager descriptions in many cases make it impossible to know how many of these tumors of the sinuses had intracranial extensions. Certainly few of the early successful cases did, for the approach universally employed was an anterior one through the orbit or upper nose until 1927, when Cushing[12] urged the necessity of an intracranial approach to those lesions extending within the cranial chamber. Successful transcranial removal of these formidable lesions has been reported in only six cases: Cushing[12] (two cases), Armitage[13] (one case from Cushing's clinic), Hoover and Horrax[14] (one case), Vincent and Mahondeau[15] (one case), Benjamins and Verbeek[16] (one case, with incomplete removal through a direct frontal sinus approach after a previous unsuccessful craniotomy). The following case may be added to this list:

Case 1.—L. B. (V. U. H. No. 82369, referred by Dr. Leo Harris, Lawrenceburg, Tenn.), a 20-year-old white farmer, was admitted December 8, 1936, complaining of pain and swelling about the left eye. Three years before he first noticed a slight, hard prominence of the left forehead. This area grew slowly, progressively more prominent. There were no associated symptoms until three months before admission, when the left eyelid became swollen. This slowly became worse and, five days before admission, he observed that the left eye was protruding and he began to have severe pain back of the eye. He vomited several times, but had no general headache and no visual disturbance. There were no other neurological symptoms. The past history and family history revealed nothing of significance.

On examination, he was seen to be a well developed young man who was in considerable pain. The tem-

*Read in Section on Neurology and Psychiatry, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

*From the Department of Surgery, Vanderbilt University School of Medicine, Nashville.

Fig. 1, Case 1
Appearance before operation. Note the protuberance of the left forehead, exophthalmos and edema of eyelids on the left.

perature fluctuated between 99 and 100.4 degrees F. and the pulse rate between 76 and 100. There were a bony hard prominence of the left forehead, marked exophthalmos on the left and extensive edema of the left conjunctiva and eyelids (*Fig. 1*). The neck was moderately stiff and Kernig's sign was present bilaterally. The general physical examination was otherwise negative. Neurological examination: He was well oriented, alert and cooperative. Memory and speech were unimpaired. The sense of smell was definitely less acute on the left than on the right. There was no papilledema and the visual acuity and fields were normal. The remaining cranial nerves were not abnormal and no motor, sensory or reflex abnormality was demonstrable in the extremities. The urine was negative, red blood count 6,430,000, white blood count 13,850 with 87 per cent polymorphonuclears. The blood Wassermann was negative, but the Kahn was positive (repeated). Cerebrospinal fluid pressure was 150 mm. of water, the fluid contained 134 white cells per cu. mm. and culture showed a few colonies of *Staphylococcus aureus*. The spinal fluid Wassermann and colloidal mastic curve were negative.

Roentgenograms showed a huge irregular bony mass occupying the expanded left frontal sinus, extending downward into the orbit and backward into the cranial cavity (*Fig. 2*).

Operation was done December 11, 1936, under tribromethyl alcohol and novocain anesthesia. A horseshoe shaped scalp flap was turned down over the left eye and cheek. Periosteum and temporal muscle were dissected down separately, disclosing the bulging anterior wall of the frontal sinus. The bone here was extremely thin and had actually been eroded through in two small areas by the smooth, ivory-like surface of the tumor which appeared in the openings. A small bone flap whose anterior edge corresponded to the posterior border of the tumor was turned down, thus allowing space for the extradural retraction of the frontal lobe. The thin anterior wall of the sinus was then chipped away. Several small pockets containing granulation tissue and mucopurulent exudate were disclosed. Smears showed no organisms (culture was later reported as containing an unidentified Gram-negative bacillus). It was then seen that one large mass of the tumor protruded downward through the roof of the orbit while another extended through the dura into the frontal lobe. The roof of the orbit was carefully bitten away with rongeurs until this extension of the tumor was free. The whole mass could then be "rocked" loose and, after further gentle retraction of the frontal lobe, the tumor was lifted from its bed (*Fig. 3*). There was no escape of cerebrospinal fluid and the intradural mass seemed to have been well walled off by fibrous tissue. A probe demonstrated the patency of the naso frontal duct. The mucosa of the sinus was curetted away and the bone flap replaced. It was fortunately possible to close the periosteum over the entire anterior bony defect except where a small gutta percha drain was inserted. This was led out through a stab wound beside the anterior limb of the incision and another wick was placed under the scalp flap posteriorly.

Course.—The postoperative recovery was excellent. A small amount of muco-sanguineous drainage from the drainage site and the nose had ceased by the fourth day, when the drain was removed. The temperature was normal by the third day. Edema rapidly subsided and there were no further signs of meningeal irritation. He was discharged on the twenty-seventh postoperative day and has remained at work and symptom-free until the present time (*Fig. 4*).

Pathology.—Grossly the tumor is a multinodular mass measuring 8 by 6 by 5 cm. Its surface is bony hard and between nodules are fragments of inflamed edematous mucous membrane and granulation tissue. When cut through the center, the cut surface shows a spongy type of bone except for a "cap" which lay in the frontal sinus. This is solid and ivory-hard. Microscopic sections show normal looking spongy bone with large marrow cavities and moderate lamellation of the solid areas.

It was with great hesitation that I proceeded with this operation in the face of the possibility of inducing a fulminating meningitis. However, it was apparent that the tumor must be removed at once if life were to be saved.

No light on the origin of these tumors can be thrown by this case. It apparently had no bony connection with the sinus wall and its size and nodular structure as well as the distortion of normal structures make any judgment on this point of little value. The fact that the frontal protrusion appeared before the orbital symptoms makes its origin in the frontal rather than the ethmoid sinus more probable.

OSTEOMA OF THE INNER TABLE

There are on record numerous cases of osteoma of the outer table of the skull and of various other primary tumors of the cranial bones (Geschickter[17]), but true osteomas arising from or protruding through the inner table are very rare.* Echlin[19] reported only three such cases in 1,000 bone tumors of the head. None of the six osteomas of the skull in Cushing's[20] 2,000 intracranial tumors is specifically said to be of this type.

*Not considered as osteomas are the hyperostoses overlying meningeal fibroblastomas or the "hyperostosis frontalis interna" of Moore.[18]

Fig. 2, Case 1
Lateral roentgenogram of the skull. The bony tumor fills the frontal sinus and protrudes into the orbit and into the cranial chamber.

Fig. 4, Case 1
Appearance of patient one week after operation.

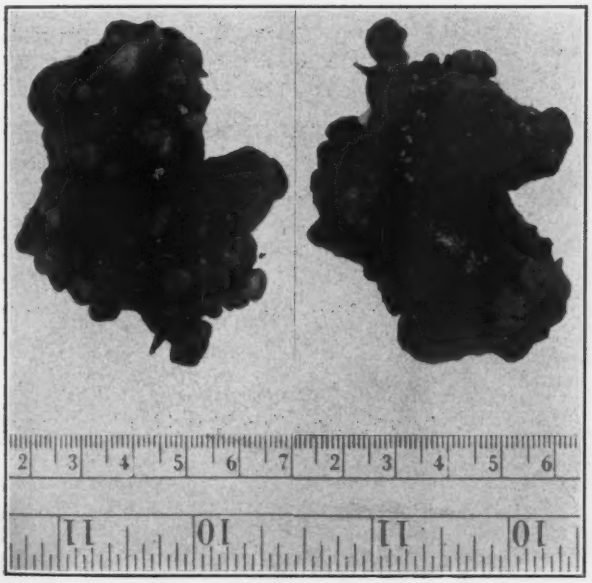

Fig. 3, Case 1
Photograph of tumor.

Case 2.—*Mrs. A. P. (V. U. H. No. 45711), a white housewife of 41, had been followed in the Vanderbilt Hospital Dispensary since October 23, 1925. She had suffered from moderately severe, infrequent "sick headaches" most of her life. At the age of 14 she had had a series of generalized nocturnal convulsions for about a year. Little could be learned of their exact nature. At the age of 30, she had spent three months in the Davidson County Tuberculosis Hospital on account of a mild pulmonary tuberculosis, which was pronounced arrested on her discharge.

On her first visit to the dispensary, she complained of a new type of headache, confined to the right side of her head, often throbbing in type and sometimes associated with tingling in the right side of her face. She was an excitable and overanxious individual who also had numerous other vague complaints, mostly

*This case and Case 3 were briefly reported in another connection in May, 1936.[21]

related to her chest. Physical examination revealed no cause for her symptoms. The lungs had apparently entirely healed. A roentgenogram made to show her sinuses, however, showed a small, nodular calcified mass in the outer portion of the middle fossa of the skull, seemingly arising from the petrous bone. This was confirmed by roentgenograms of the skull.

She was seen by various observers, none of whom believed that the intracranial mass was the cause of her symptoms, and she was followed at intervals largely with regard to her chest condition. The headaches continued, but did not incapacitate her, and she began to have occasional mild ringing in her right ear. On October 5, 1931, roentgenograms of the skull showed that the mass was definitely larger than before, and she was advised by Dr. T. D. McKinney to have it removed. She refused operation, however, and did not return until February 2, 1932. The previous night she had had a generalized convulsion characterized by loss of consciousness, biting of her tongue, turning of her head to the left and clonic spasm of all extremities.

She was admitted to the hospital on the medical service and after careful study, including normal findings in the cerebrospinal fluid, her physicians again felt that her symptoms were probably not related to the intracranial mass. During the next two years she had about twenty nocturnal convulsive seizures, the headaches and tinnitus continued without much change, and she stated that her memory for recent events was becoming poor. No neurological signs appeared.

Her pulmonary condition remained unchanged, but, when she became pregnant for the third time in ten years, it was thought wise to terminate the pregnancy by cesarean section and to sterilize her, lest the burden of repeated pregnancies cause a flare-up in her tuberculosis. This was done by Dr. W. L. Williams on December 20, 1933. She made a satisfactory recovery and was again followed in the clinic.

I first saw her on February 23, 1935. At this time she had begun to have occasional "dreamy state" attacks, in which she would suddenly go blank for a moment and have a feeling of being transported out of her body. These attacks were not accompanied by hallucinations of smell or taste. Her eyegrounds were normal, but she had a left facial weakness, and her tongue protruded to the left. The tendon reflexes were uniformly hyperactive. There was no defect of speech, although she was left-handed. X-rays of the skull showed a further increase in the size of the bony mass within the skull (*Fig. 5a*).

She was again advised to have the tumor removed, and went home to think it over, but it was not until October 18, 1935, that she returned for the operation.

At operation, October 24, 1935, a large right temporal bone flap was turned down. The large, nodular, bony mass was growing from a broad base which was fortunately in the lower portion of the squamous, rather than the petrous, portion of the temporal bone. It had forced the temporal lobe of the brain upward until the sylvian fissure lay half way up the convexity of the hemisphere. The dura mater was so incorporated in the base of the tumor that it was necessary to approach it intradurally. By careful dissection, the tumor was finally freed from the brain, and it was possible to cut completely around the mass with an osteotome, thus removing the entire tumor and its base in the temporal bone in one mass (*Fig. 6*).

Course.—She made a rapid recovery and was discharged from the hospital free of symptoms on the twelfth postoperative day (*Figs. 5a* and *7*). There were no further symptoms until April 4, 1936, when she had a single fleeting "dreamy spell." Except for this, there have been no symptoms until the present time. She is completely free of headache.

Pathology.—The tumor is an ivory-hard nodular mass with smooth surface on its intracranial side. When cut through the center, its surface is equally smooth, hard and homogeneous except at the base, where there is spongy bone corresponding to the diploë of the cranium, although it is much thicker. A fragment of the dura be-

Fig. 5-a, Case 2
Roentgenogram of skull prior to operation, showing the bony tumor in the temporal fossa.

Fig. 5-b, Case 2
Roentgenogram of skull after removal of tumor.

neath this tumor layer seems to disappear into the tumor, as though the latter had grown through it. Microscopically, the tumor is a typical "osteoma eburnea" with few haversian canals, heavy lamellae coursing in different directions and no marrow spaces.

A fascinating question in this case is the relation of the tumor to the dura. Its origin from the skull can hardly be questioned, yet it somehow managed to give the appearance of protruding through the dura. It seems probable that it simply greatly stretched and perhaps finally destroyed the dura in front of it, while the dura at its margins had meanwhile become incorporated in the edges of the tumor itself.

Fig. 6, Case 2

Photograph of tumor. The thread at left is in the dura, which seems to be incorporated between the tumor and its thick base in the temporal bone.

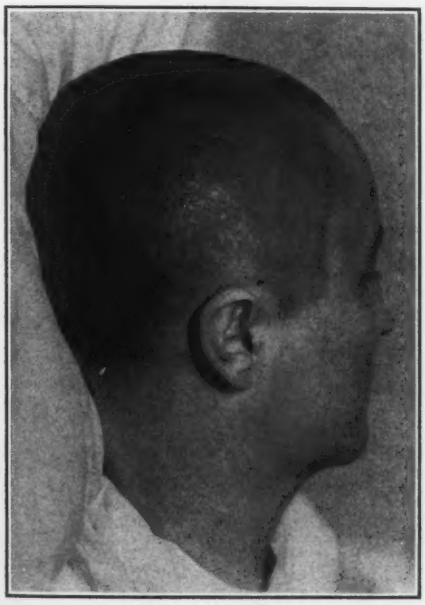

Fig. 7, Case 2

Appearance of patient ten days after operation.

From the clinical point of view, there can be little doubt that the tumor was the cause of the patient's symptoms during the ten years prior to operation. Whether it bore any relation to her childhood convulsions cannot be stated. That the tumor could and should have been removed many years before is evident. Since this paper was prepared, two additional osteomas of the inner table have been seen. One, in the left frontal region, was successfully removed. The other, also left frontal, which had been the cause of no symptoms, was discovered as an incidental finding and has not been operated upon. A study of similar "enostoses" in a museum collection of skulls has been published since preparation of this paper by Canavan.*

INTRADURAL BONY TUMOR

Many types of cerebral neoplasm contain deposits of calcium and sometimes of bone, often sufficiently extensive to be roentgenologically demonstrable. Further, there are recorded a number of cases of osteochondroma containing varying amounts of bone believed to originate in the meninges (Alpers,[22] Wolf and Echlin[23]). All neurosurgeons have seen the calcified plaques in the spinal and, less frequently, in the cerebral arachnoid. In 1860, Wilks[24] reported a solid bony plate attached to the spinal arachnoid. Microscopically, the structure was

> "for the most part fibrous * * * sometimes true bone may be met with, having well formed lacunae, canaliculae, etc. * * *"

Very few true bony tumors within the cerebral dura have been reported (Ewing[25]). One remarkable specimen, removed at necropsy and described by Laignel-Lavastine and Liber,[26] contained a large, cystic tumor ("angioma") of the cerebellum. In addition, between the hemispheres there were large, symmetrical bony masses on each side of, and apparently attached to the falx cerebri. Microscopically, they were composed of spongy bone. Similar in many respects is the following case:

Case 3.—Mrs. K. J. (V. U. H. No. 76661, referred by Dr. C. F. Hartung, Jr., of Bridgeport, Alabama, and Dr. Albert Weinstein, of Nashville, Tennessee), a white housewife of 39, was admitted February 13, 1936. She had had intermittent severe headaches most of her life, particularly at the time of her menstrual periods.

*Arch. Neurol. & Psychiat., **38**:1240, 1937.

She had always been "nervous" and intense and, for four years before admission, had been known to have periodic elevations of blood pressure, which sometimes rose as high as 250 millimeters systolic. She had always vomited with very little apparent provocation and had had four therapeutic abortions for the vomiting of pregnancy.

In 1930, she was struck in the head by a falling elevator gate without apparent significant effect. One year before admission her head was struck on the right side in an automobile accident. Following this, she began to have much more severe and frequent headaches, which seemed to begin over the right eye and extend over the top of her head to the right occipital region. It was observed that her "nervousness" gradually increased, and relatives believed she showed definite early personality changes characterized by absent-mindedness, irritability and a sort of childishness of speech and manner. The headaches became so severe that narcotics were required for relief.

On admission, she was found to be jumpy, excitable, and suffering with severe pain in the right side of the head. The head revealed nothing abnormal. The eyegrounds were normal. The general and neurological examinations were entirely negative except that the blood pressure varied on several examinations from 154/94 to 190/115. The urine and blood were normal, the Wassermann negative. The spinal fluid was under a pressure of 260 millimeters of water, but was otherwise normal. Roentgenograms of the skull showed a large, irregular, fluffy-looking area of calcification extending from the midline out over the right hemisphere (*Fig. 8*). Whether it was a growth from the inner table of the skull or lay deeper could not be determined. The blood calcium and phosphorus were found to be normal.

The first operation was done February 17, 1936. It seemed wise first to determine the nature and depth of the intracranial calcification. Accordingly, a small trephine opening was made in the right frontal region. The inner table was normal in appearance, but within the dura was a solid, bony mass which obviously would require an extensive craniotomy for its removal.

Fig. 8, Case 3
Lateral roentgenogram of skull showing the irregular serrated calcification in the right frontal and parietal region.

At the second operation, February 19, 1936, under tribromethyl alcohol and procaine hydrochloride anesthesia, a large, right-sided bone flap, extending across the midline, was turned down. The inner surface of the dura was adherent to the large, irregular, underlying bony mass, but it was finally dissected free up to the superior longitudinal sinus. The mass could then be seen to be a wide, flat plaque of bone, thickest next to the sinus and growing thinner as it extended farther laterally. At its widest point it was about four centimeters in width and its length was about fifteen centimeters. Several smaller separate peripheral plaques were also present. The bony masses were lightly adherent to the cortex, but, by careful dissection, could be separated and elevated enough to allow their removal bit by bit with the rongeur (*Fig. 9*). The final narrow strip along the sinus could fortunately be stripped away without tearing the sinus wall. There was no point of firm attachment, but the increasing thickness medially suggested an origin near the sinus. A small amount of similar bone could be palpated through the dura on the left side, but it was not thought wise to perform the extensive operation which would have been necessary for its removal.

Course.—The wound healed rapidly, and, except for troublesome vomiting for a few days, the patient made an uneventful recovery. Surprisingly, her blood pressure fell to a level of 140 mm. systolic which was maintained. She remained completely free of headache until April, 1937 (14 months after operation), when her physician reported a brief attack of severe headache with vomiting. This improved and she did not return for examination. Her blood pressure at that time was not reported.

Pathology.—Microscopically, the pieces of the calcified plaque are composed of true spongy bone with large marrow spaces and normal cellular constituents.

This lesion was similar to that of Laignel-Lavastine and Liber[26] in that it lay along the falx on both sides and it contained true bone. It differs in having extended out over the cortex rather than down between the hemispheres. The origin of this bony mass is difficult to explain. Presumably, as suggested by Alpers[22] in his case

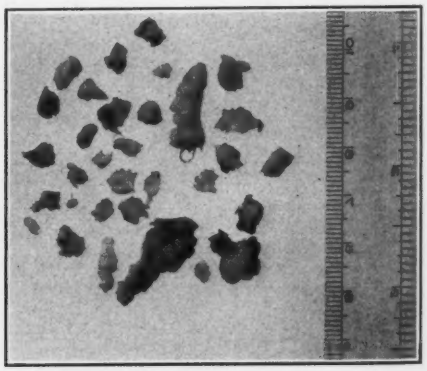

Fig. 9, Case 3
Photograph of the fragments of the bony mass removed.

of osteochondroma and by Ewing,[27] it must have arisen from meningoblastic cells.

SUMMARY

Examples of three unusual types of intracranial bony tumor, with successful removal, are reported:

(1) Osteoma of the frontal sinus with extension into the orbit and the cranial chamber.

(2) An osteoma arising from the inner table of the temporal bone and protruding through the meninges into the temporal lobe.

(3) A bilateral intradural bony growth.

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RUPTURE OF BICEPS BRACHII*

REPORT OF 14 CASES

By RICHEY L. WAUGH, M.D., F.A.C.S.
New Orleans, Louisiana

The purpose of presenting this paper is to emphasize the fact that rupture of the biceps brachii occurs more frequently than is generally supposed. Ruptures of this tendon or muscle often go unrecognized and undiagnosed, probably due to the fact that there are many practitioners as well as general surgeons who are unfamiliar with the symptoms and signs of this condition.

Petit,[1] in 1722, was the first to report a case of a rupture of a muscle. However, the first known reference to rupture of the biceps brachii was that made by Rouselle Chamseru[2] in 1781. Since then quite a number of contributions have appeared in various journals here and abroad. Of these, the papers by Gilcreest[3 4 5 6] are the most outstanding. Strangely, most of the textbooks on surgery, with the exception of Christopher,[7] have given this subject little or no mention.

There were six patients with rupture of the biceps brachii among a total of 20,088 patients admitted to the Marine Hospital, San Francisco, during the six years, 1929 to 1935. Eight patients with this same condition, among a total of 8,667, have been admitted to the Marine Hospital, New Orleans, during the past two years. The recognition of these last eight cases may be due to the "biceps mindedness" of the intern staff, for there was no diagnosis of this condition among 22,499 admissions to the New Orleans hospital during the previous six years.

Haldeman and Soto-Hall[8] state that the statistics completed by Grassheim on 500 cases show that the muscles and tendons most frequently ruptured are those of the calf group, extensors of the leg, biceps brachii, achilles tendon and thumb extensor in the order given.

Codman,[9] reporting 500 cases of shoulder injuries, found 122 cases of rupture of the supraspinatus and only 9 cases of rupture of the biceps. He found that the biceps is frequently injured with the supraspinatus and was of the belief that this fact frequently misled many surgeons to attribute supraspinatus symptoms to those due to the associated biceps rupture. In

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*From the Surgical Services, U. S. Marine Hospital, San Francisco and New Orleans.

his opinion, rupture of the tendon of the long head of the biceps alone is a trivial matter, but when combined with an injury to the supraspinatus becomes very serious because of the help of the long tendon in maintaining the head of the humerus against the glenoid cavity.

All of our ruptured biceps cases were actively engaged in laborious work, the majority (70 per cent) being merchant seamen. The ages varied from 39 to 62 years, with an average age of 48½ years. This is in agreement with other writers who make the general statement that these lesions occur most often in men over 40 years of age, at a time when wear and tear of the muscles and tendons secondary to degenerative and pathologic changes are more likely present.

Gilcreest[6] states that excessive fatigue may render muscle fibers less likely to resist a sudden and forceful pull or jerk, and that fatigue superimposed upon other predisposing factors may cause rupture more easily. He cites the case of Loos, a man of 70, who upon returning home after long and wearisome work, raised his arm to take off his hat and in so doing ruptured his left biceps. Gilcreest[6] also refers to the immortal and versatile John Hunter, who became interested in the mechanics of muscle ruptures after having sustained a rupture of his gastrocnemius while dancing. In discussing the mechanics of a ruptured muscle, he quotes Hunter in part: "A broken tendon usually arises from the power of a muscle being put into full action and a sudden resistance taking place at the same time." In this connection, there might be added the name of Charles H. Mayo,[10] who, while running upstairs two steps at a time, slipped and fell forwards, rupturing his soleus muscle.

The sudden contraction of the biceps brachii sufficient to rupture the tendon or muscle more frequently occurs as a result of sudden or uncoordinated movements such as lifting while in an awkward or strained position. Gilcreest,[6] however, states that a fall on the shoulder, usually considered a form of direct trauma, may throw a great strain on the long tendon and in this way may indirectly produce such a rupture.

In our series of 14 cases, seven were due to indirect trauma and 4 were due to direct trauma.

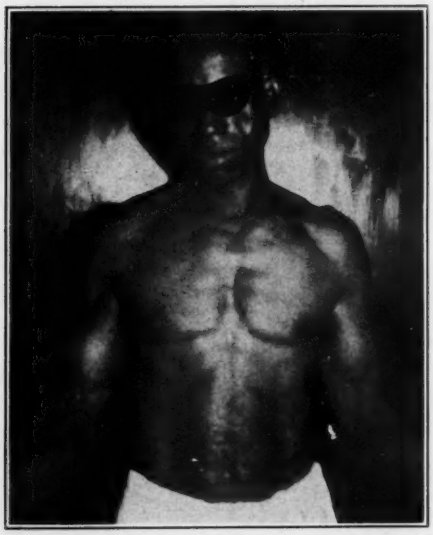

Fig. 1, Case 7

While lifting filing cabinets, the patient felt sudden pain in the right shoulder and the arm "gave way." Since then he had pain and weakness of the right arm and was unable to work. Operation eight days after injury revealed long tendon avulsed at glenoid rim. Note "plateau" appearance of biceps with forearm partially extended.

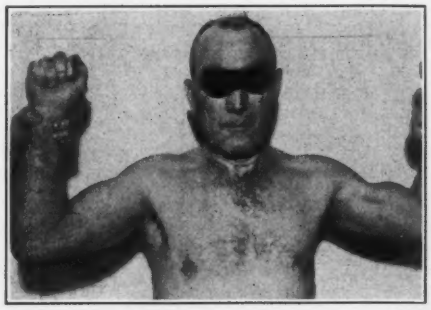

Fig. 2, Case 8

While at sea the patient struck his left shoulder against a steam valve. Next day the shoulder was stiff and painful. He had constant weakness and a "catch" in the left shoulder and arm. Operation three months after injury revealed the long tendon elongated, but fixed in groove.

Fig. 3, Case 9

While working as deck hand and lifting a heavy plank, the patient suffered a sudden "jerk" to the right elbow, resulting in painful swelling and weakness of the right arm. Operation six weeks after injury revealed rupture of the distal tendon.

The remaining three are not considered as the mode of injury was uncertain in two and in the other a stabbing injury was the predisposing cause. Syphilis is said only rarely to be the cause of a muscle rupture. Although of doubtful significance, three of the patients (21 per cent), not including the one due to the stabbing injury, gave a positive blood Wassermann reaction. It also is interesting to note that in these three patients, the mode of injury was indirect, that of lifting. Also these three patients with the positive blood Wassermann reactions represent over 40 per cent of the group sustaining biceps muscle rupture by indirect means.

The biceps brachii may rupture at almost any site. Biancheri[11] reported that the long head and its tendon are most frequently affected, 96 per cent; next, the lower tendon, 3 per cent; and least of all, the short head, 1 per cent. In our series, 12 of the 14 cases (85 per cent) were of the long head and its tendon, and 2 (14 per cent) were of the lower tendon. Gilcreest[6] found in the literature only 19 cases of rupture of the lower tendon and added 3 more from his series (Holcomb's, Simpson's and his own). Since then it appears that only one other case (Leavitt and Clements[12]) has been reported. That case, together with our two, brings up the total reported cases of rupture of the lower tendon to twenty-five.

In rupture of the long tendon there are two types, the high and low. The high type is the usual type and ordinarily results from predisposing degenerative changes. The low type, ruptures at or slightly below the level of the bicipital groove. This type, as borne out by our cases, is more often found following direct trauma. In some instances, there is a gradual fraying out

Fig. 4, Case 10

Mode of injury is uncertain, but the patient gave a history of a fall three years before and again sixteen months before admission and operation. Symptoms were pain and weakness of the right arm. At operation only a thread of long tendon remained, the belly of muscle was in a "ball" and there was much scar tissue at the site of the musculotendinous junction. There was a partial recurrence of the deformity after operation. Function of the arm was improved and he declined further operation.

Fig. 5, Case 11

While at sea a steel door flew open, striking the left shoulder of the patient. The shoulder and arm became "black and blue." Two days after injury he noticed a "lump" in the left arm. There was weakness of the arm from the time of injury. Operation eleven months after injury revealed scar tissue replacing long tendon at musculotendinous junction.

6a

6b

Figs. 6a and 6b, Case 13

While lifting a sack of sugar to his shoulder the sack slipped and he "strained" his right shoulder. Afterwards he noticed pain, swelling and weakness of the right arm. Operation two years after injury revealed elongation of long tendon and much scar tissue at the upper musculotendinous junction. (a) Before operation. (b) After operation.

of the tendon in the bicipital groove, followed by adhesions sufficiently strong to hold the tendon, but there results an elongation of the tendon with the usual bicipital syndrome. A lesion of this type is frequently unrecognized, undiagnosed and untreated.

The symptoms and signs in our series were variable. All patients, however, gave a history of trauma followed by pain in the shoulder and arm. The chief complaints were weakness of the arm and discomfort in the shoulder. Two patients gave a history of ecchymosis. The most constant sign was a deformity, particularly a change in the contour of the region of the biceps. The deformity, bunching of the belly of the biceps due to shortening of the severed fibers, was marked if the rupture of the upper tendon was complete or if the rupture was at the upper musculotendinous junction. The bunching also varied as to location and was found closer to the elbow when the rupture site was in the long tendon and closer to the shoulder when in the lower tendon. It also has been our observation that in upper tendon rupture, of the complete and hightype, the muscle bunching assumes more of a "plateau" appearance with the elbow partially extended. When the long tendon is ruptured, the short head naturally becomes more prominent, a hollow or depression is seen, and the long tendon may be palpated either coiled or in a slackened state. Frequently tenderness was localized in the region of the bicipital groove. The degree of impairment of function of the arm and shoulder varied from a slight weakness to a moderate loss of function. Of the various signs, Hueter's[13] sign was recorded in 6 cases (43 per cent), Ludington's[14] sign was recorded in 5 cases (35 per cent), and Yergason's[15] sign was recorded in one case (7 per cent).

Hueter's sign: Flexion of the forearm in pronation when the biceps is tense is more forcible than when the forearm is supinated and the biceps relaxed.

Ludington's sign: The patient is directed to rest his folded hands palms down, on the top of his head and allow the interlocked fingers to support the weight of the arms. In this position there is maximum relaxation of the long head. The examiner then places two fingers on the tendon of the long head of the biceps, and directs the patient to contract and relax the biceps muscle simultaneously. The contraction of the tendon of the long head on the sound side is felt plainly, while it is absent on the affected

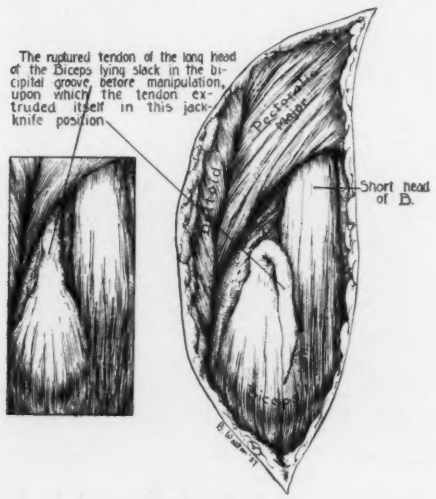
The ruptured tendon of the long head of the Biceps lying slack in the bicipital groove, before manipulation, upon which the tendon extruded itself in this jack-knife position
Pectoralis Major
Short head of B.

Fig. 7, Case 7
Operative findings.

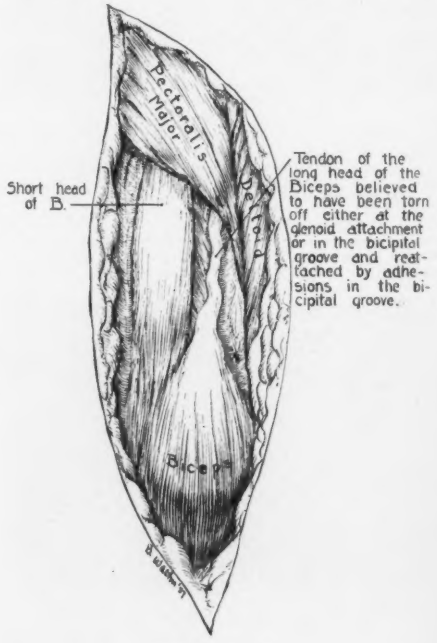
Pectoralis Major
Short head of B.
Tendon of the long head of the Biceps believed to have been torn off either at the glenoid attachment or in the bicipital groove and reattached by adhesions in the bicipital groove.
Biceps

Fig. 8, Case 8
Operative findings.

side if the tendon is ruptured or is felt less readily if the tendon is elongated.

Yergason's sign: If the elbow is flexed to 90 degrees, the forearm being pronated, and the examiner holds the patient's wrist so as to resist supination and then directs that active supination be made against his resistance, pain, very definitely localized in the bicipital groove, indicates a condition of wear and tear of the long head of the biceps or synovitis of its tendon sheath.

Naturally the character of the treatment will depend upon the severity as well as the site of the rupture. If the rupture is partial with little deformity and only slight impairment of function, good results should be expected from conservative measures. However, for most cases operation is the method of choice.

Gilcreest[6] is quite in accord with Keen's[16] statement that "it seemed strange to him that surgeons have so rarely operated on these patients when one sees so many cases of impaired function in those not operated on and such good results in those operated on early." Ludington[14] is no less emphatic in stating that the proper treatment is operation. He states that palliative measures offer no prospects of relief and that the disability is permanent unless corrected by operative means.

If the long tendon is ruptured at its attachment to the lip of the glenoid or near its upper end and there is sufficient tendon, one of several methods of repair may be chosen: (1) suture to the short head, (2) suture to the corocoid process, (3) suture to the bicipital groove, and (4) suture to either the deltoid or pectoralis major muscle.

We quite agree with Gilcreest[8] that if there is sufficient tendon it is better to combine the first two methods, i. e., slipping the long tendon through and suturing it to a portion of the short head, and also suturing the end of the tendon to the corocoid process. In one of our cases after weaving the long tendon through the short

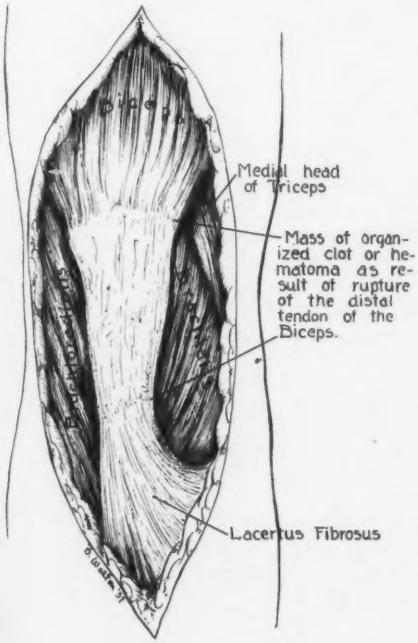
Biceps
Medial head of Triceps
Mass of organized clot or hematoma as result of rupture of the distal tendon of the Biceps.
Lacertus Fibrosus

Fig. 9, Case 9
Operative findings.

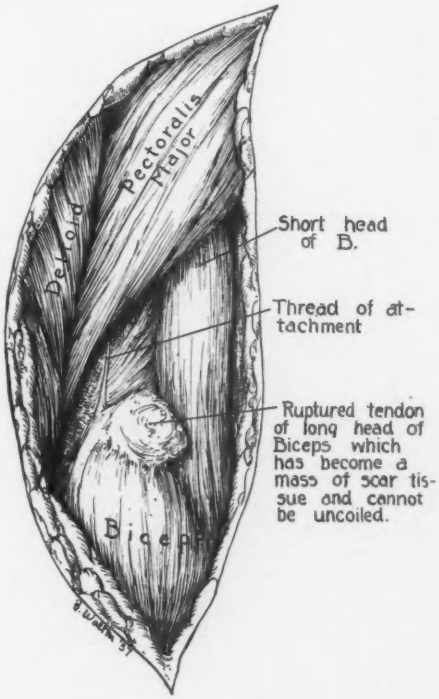
Pectoralis Major
Deltoid
Short head of B.
Thread of attachment
Ruptured tendon of long head of Biceps which has become a mass of scar tissue and cannot be uncoiled.
Biceps

Fig. 10, Case 10
Operative findings.

SUMMARY OF CASES

RUPTURE OF BICEPS BRACHII

Case	Age	Work	Time Lapse	Injury	Wassermann	Side Affected	Symptoms	Signs	Operative Findings	Nature of Operation	Result
1	53	M.S.	13 yrs.	Dir.	—	L	History of "tearing pain" in shoulder. Pain, weakness	Bunching. Subdeltoid depression	Separation at upper musculotendinous junction and much scar tissue	Scar tissue of muscle sutured to tendon, chromic sutures	Good
2	54	M.S.	5 mos.	Ind.	—	L	History of "tearing pain" in shoulder. Pain, weakness	Bunching. Subdeltoid depression Roentgenogram-hypertrophic changes	Long tendon lax and adherent in groove and tendon frayed at joint capsule	Long tendon sutured to short head and to coracoid process, chromic sutures	Good
3	48	M.S.	7 wks.	Ind.	+	L	Pain, weakness	Bunching. Subdeltoid depression. Hueter's and Ludington's signs positive. Roentgenogram-hypertrophic changes	Long tendon ruptured at glenoid rim and folded upon itself in groove	Long tendon sutured to short head and to coracoid process, chromic sutures	Good
4	41	M.S.	1 yr.	Dir.	—	L	History of ecchymosis. Pain, weakness	Bunching. Subdeltoid depression. Hueter's and Ludington's signs positive	Partial rupture upper musculotendinous junction	Scar tissue of muscle sutured to tendon, chromic sutures	Good
5	51	Lab. (CWA)	2 days	Ind.	—	L	History of "snap in shoulder" and tingling in arm. Pain, weakness	Ecchymosis, bunching, subdeltoid depression	Long tendon ruptured at glenoid rim and end of tendon frayed out in "fan" shape	Long tendon sutured to short head and to coracoid process, silk sutures	Good
6	62	Lab. (CWA)	6 yrs.	?	—	L	Pain, weakness	Bunching. Subdeltoid depression	Not operated upon	Not operated upon	Not operated upon
7	47	Lab. (ECC)	8 days	Ind.	+	R	Pain, weakness	Bunching. Tenderness over groove	Long tendon ruptured at glenoid rim	Long tendon sutured to short head and to coracoid process, chromic sutures	Good anatomically, but with impaired function(?) (compensation case)
8	50	M.S.	3 mos.	Dir.	—	L	Pain, weakness	Bunching Tenderness over groove. Yergason's sign positive. Hueter's sign positive	Long tendon elongated, but fixed in groove	Long tendon carried through short head and drill hole in coracoid process, silk sutures	Good
9	39	M.S.	6 wks.	Ind.	+	R	Pain, weakness	Bunching (proximally), tenderness, thickening site distal tendon	Distal tendon ruptured above lacertus fibrosus	Partially organized clot removed and defect spanned by 3-ply fascia lata transplant, chromic sutures	Good, but distal tendon too slack

SUMMARY OF CASES—(Concluded)

RUPTURE OF BICEPS BRACHII

Case	Age	Work	Time Lapse	Injury	Wassermann	Side Affected	Symptoms	Signs	Operative Findings	Nature of Operation	Result
10	40	M.S.	Over 16 mos.	?	—	R	Pain, weakness	Bunching. Slight tenderness. Hueter's sign positive. Ludington's sign positive	Long tendon only a thread; belly of muscle in a "ball" and scar tissue site of musculotendinous junction	Scar tissue of muscle belly sutured to short head, chromic sutures	Partial recurrence, but function of arm improved (fascia lata transplant should have been used in repair). Declined further operation
11	59	M.S.	11 mos.	Dir.	—	L	History of ecchymosis. Tingling sensation in ring and little fingers. Increased weakness	Bunching Slight tenderness. Hueter's sign positive. Ludington's sign positive	Scar tissue replacing long tendon at musculotendinous junction and belly of muscle prominent	Fibrosed cord of long tendon separated from adhesions and sutured to short head and to coracoid process, silk sutures	Good
12	44	Lab. (VB)	3 yrs.	Dir. (Stab)	+	R	Weakness. Tingling sensation in ring and little fingers	Scar visible subdeltoid region. Bunching (irregular). Hueter's sign positive. Ludington's sign positive	Scar tissue and adhesions under deltoid involving partially divided long tendon	Dissection and suture of scar tissue to tendon, silk sutures	Good, but complained of numbness of little finger
13	43	M.S.	2 yrs.	Ind.	—	R	Pain, weakness	Bunching. Subdeltoid depression	Long tendon elongated. Scar tissue at upper musculotendinous junction	Long tendon sectioned above scar tissue at upper musculotendinous junction and reattached by weaving through and suturing to scar tissue	Good
14	50	M.S.	1½ yrs.	Ind.	—	R	Slight weakness	Bunching (proximally). Thickening site distal tendon	Not operated upon	Not operated upon	Not operated upon

head, the end of the tendon was fastened through a hole drilled in the corocoid process. This gave not only a high, but a very firm attachment.

If the rupture is of the low type or of either the upper or lower musculotendinous junction, it may be necessary to resort to fascial transplant or other plastic procedure. For ruptures of the lower tendon several methods of repair have been followed. Kirschner[17] employs fixation of the tendon to the radius with a nail or, if this is not possible, he sutures the tendon to the neighboring soft parts. Leavitt[12] scarifies the periosteum and reattaches the distal tendon by a hole drilled through the margin of the bicipital tuberosity. Bauman[18] demonstrated a method of suturing the distal tendon by transfixing the tissues with sutures from the end of the tendon to the posterior forearm, where they are tied over gauze to hold the tendon in place. It would seem that fascial transplant fixation by drill holes through the radius offers the most dependable attachment. In our series the time elapsing between date of injury and date of operation varied from two days to thirteen years.

Contrary to the uniformly good results following operation reported by other writers, in our series there have been two cases in which the results have not been entirely satisfactory. In one, Case 9, operated upon 6 weeks after injury, the fascia lata transplants used to span the defect in the distal tendon were sutured with the forearm in supination and the elbow in a position of about 90 degrees flexion. The result was noticeable slackness of the reconstructed distal tendon when the elbow was extended, yet little, if any, impairment of elbow function. This slackness, of course, could have been prevented by increasing the degree of elbow flexion at the time of the fascia transplant suture. In the other, Case 10, operated upon 16 months after injury, the old atrophic coiled-up tendon could not be uncoiled. The error was made in attempting repair by means of suture of the scar tissue to the sheath and muscle of the short head. Although function was improved, there was partial recurrence of the deformity. This, no doubt, could have been prevented by the utilization of a fascia transplant for the reconstruction of a new tendon attached to the corocoid process.

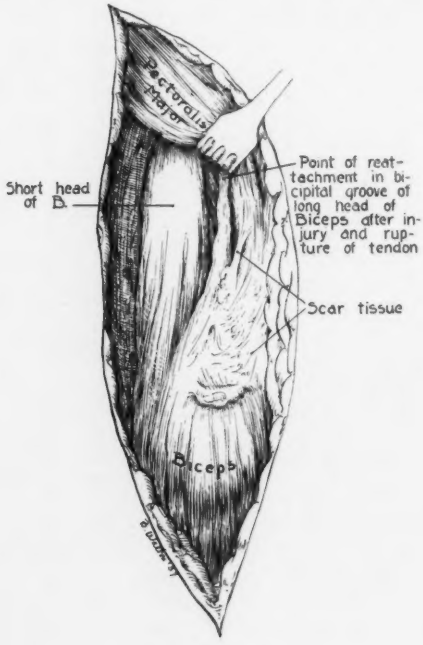
Pectoralis Major
Short head of B.
Point of reattachment in bicipital groove of long head of Biceps after injury and rupture of tendon
Scar tissue
Biceps

Fig. 11, Case 11
Operative findings.

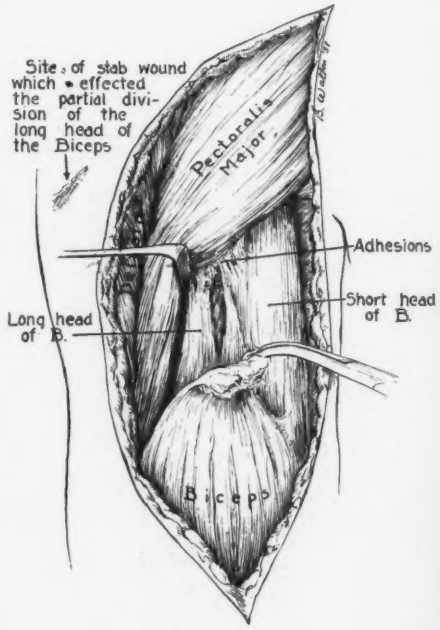
Site of stab wound which effected the partial division of the long head of the Biceps
Pectoralis Major
Adhesions
Short head of B.
Long head of B.
Biceps

Fig. 12, Case 12
Operative findings.

As an adjunct to treatment, either operative or conservative, proper position of rest or fixation is important in order to obtain maximum relaxation and approximation of the torn muscle or tendon. The position must be such that, if stiffness occurs, it will disable the patient as little as possible. Further, the position must be one which will be advantageous to start from in securing a wider range of movement. Such optimum position is that described by McGregor,[19] comparable to the position of military salute in which the arm is in mid-abduction and external rotation, the forearm in mid-position and the elbow flexed to about 115 degrees.

SUMMARY

(1) A report of 14 cases of rupture of the biceps brachii is presented. The frequency, the mechanism, the sites and types of rupture, the symptoms and signs, the method of treatment and the results of treatment of the cases in this series are analyzed and are compared with those of other writers.

(2) The point is made that rupture of this tendon or muscle often goes unrecognized and undiagnosed, probably due to the fact that many practitioners as well as general surgeons are unfamiliar with the symptoms and signs of this condition.

(3) During a period of 6 years, there were 6 patients with rupture of the biceps brachii admitted to the Marine Hospital, San Francisco, among a total of 20,086 admissions. Eight patients with the same condition among a total of 8,667 admissions have been admitted to the Marine Hospital, New Orleans, during the past two years. The recognition of these last 8 cases is believed due to the "biceps mindedness" of the interne staff, for there was no diagnosis of this condition among 20,499 admissions to the New Orleans hospital during the previous six years.

(4) All patients were actively engaged in laborious work, 70 per cent being merchant seamen. Indirect trauma such as lifting, straining, etc., as the exciting cause of the rupture was about twice as common as direct trauma.

(5) Twelve of the 14 cases (85 per cent) were of the long head and its tendon and 2 cases (14 per cent) were of the lower tendon.

(6) Our 2 cases of rupture of the lower tendon with the 23 cases found in the literature brings up the total reported cases of rupture of lower tendon to 25.

(7) The observation is made that in upper tendon rupture of the complete and high type, the muscle deformity (bunching) assumes a "plateau" appearance with the elbow partially extended.

(8) Twelve of the 14 cases were operated upon. The time elapsing between date of injury and date of operation in the 12 cases varied from 2 days to 13 years.

(9) The character of the treatment depends upon the degree and site of the rupture. Conservative treatment is indicated in partial ruptures, with little deformity and only slight impairment of function. For most cases, operation is the method of choice. Ruptures of the long tendon of the complete and high type are easily repaired and the results are highly satisfactory, particularly if operated upon early. Ruptures at musculotendinous junctions or of the lower tendon are more difficult to repair and the results are less satisfactory. For these cases, fascial transplant or other plastic procedure is recommended.

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CONGENITAL LUNG CYSTS, AIR EXPANSILE TYPES*

By Wm. Willis Anderson, M.D.
Atlanta, Georgia

The type of air expanding lung cyst discussed below is assumed to be congenital in origin, although this is not definitely proven. It has a beginning as an intrapulmonary fluid sac, the walls of which are made up of secreting bronchial epithelium. At various times, more particularly during pulmonary infections, as pneumonia, the fluid cyst increases in size very rapidly until it ruptures into a neighboring bronchus. An air trap is then formed, allowing air to enter the cyst but not escape.

Report of instances of two infants coming under observation during the past year, one in detail, because he was studied prior to the formation of the air cyst, at the time of the development of the expanding air cyst, and at autopsy, is given with a review of some of the other recent reports of congenital lung cysts.

King and Harris[1] recently studied reports of 152 congenital lung cysts occurring since 1925, adding two instances of this type of expanding lung cysts coming under their observation. That the condition is being recognized clinically with increasing frequency, due largely to increased efficiency in improved methods of roentgenological technic, is evidenced by the fact that prior to 1925, Koontz[2] was able to collect from the literature of the world at large only 108 autopsy reports of congenital lung cysts of all types. Since congenital lung cysts increase most rapidly in size during pulmonary infection, it is possible that even more might be recognized if more roentgenological examinations were made on atypical pulmonary infections at the end of the disease as well as at the beginning and during the acute stages.

The following patient, H. R., a Negro boy, 11 months of age, is of interest in that he was observed at birth, in the out-patient department of Emory University Division of Grady Hospital, during a previous admission to the hospital and at autopsy. He was admitted last to the hospital on December 14, 1936. His mother complained that he was "sore all over, held his neck stiff and had a cough."

His family history was negative for tuberculosis, syphilis and other diseases of a familial tendency. He weighed 9 pounds at birth. The birth was normal. Wassermann reactions of the mother's blood and blood from the umbilical cord were negative.

May 18, 1936, when he was 3 months of age, he was admitted to the hospital with pneumonia. A roentgenologic examination of his chest on the day of his admission revealed in both posterior-anterior and direct lateral exposures scattered, patchy areas of consolidation throughout both lungs. On studying the films at the time, and since, Dr. Wm. Bryan noted no lung cyst. The patient spent nine days in the hospital. A tuberculin (0.01 mg. old tuberculin) skin test was negative. His white blood count was 12,400. On physical examination the percussion note was impaired at the left upper chest anteriorly, where a few moist rales were heard. His rectal temperature ranged from 99 to 101° F., usually being about 100° F. His general condition improved, although when he was discharged May 26, 1936, an occasional rale could be heard at the left upper, and the percussion note was impaired. No roentgenologic examination was made at the time he left the hospital.

When he re-entered the hospital in December, 1936, his mother said that he had been ill for about two weeks. He would scream with pain when picked up, and had a stiff neck. She thought that his body temperature had been elevated during this time. (She had consulted her family doctor, who had given him an injection into the buttock and an ointment to rub into the axillae.)

On examination his rectal temperature was 103°, his pulse 120 per minute and his respirations were 20 per minute. The chest revealed a moderate impairment of

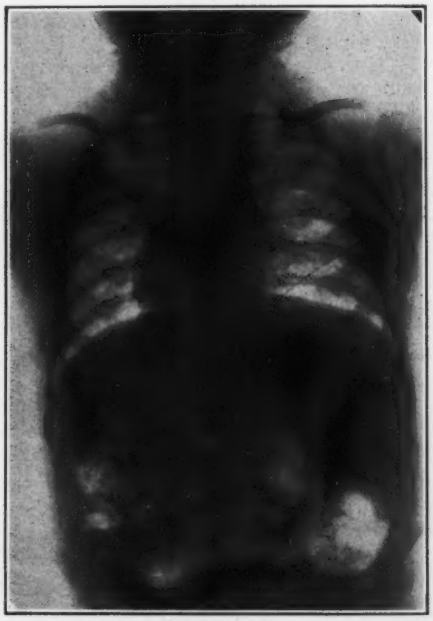

Fig. 1
Pneumonia, May 1936, prior to development of air expanding lung test.

*Read in Section on Pediatrics, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

percussion note at the apices of both lungs anteriorly. Moist rales were heard at the left upper front and high up in the right axilla. His cardiac dullness was obscured by pulmonary dullness on the left side. The sounds were normal in character.

Examination of his abdomen revealed an umbilical hernia the size of a large acorn. Otherwise, it was normal.

He had a tendency to lie constantly on the left side with the legs flexed, which subsequently proved to be due to the site of the injection in his buttocks. This showed increased tenderness and swelling and was aspirated on January 5, 1937, a "sterile" yellow, greenish pus being obtained. Roentgenologic examinations of the bones of the hip and pelvis were negative.

A single lumbar puncture showed a clear, colorless fluid not under increased pressure, containing 4 cells per cu. mm. Smears, a culture and Wassermann reactions were negative. Skin reactions of both 0.01 mg. of old tuberculin and 1.0 mg. were negative. Six urinalyses revealed an occasional granular cast and occasional trace of albumin. Wassermann reactions of the blood were negative. Four sputum examinations for acid fast bacilli were negative. One blood culture, taken on December 31, 1936, was contaminated with staphylococci. Three subsequent cultures were negative. Examination of the blood revealed 3,720,000 erythrocytes, white blood cells 20,200 with neutrophils 68 per cent.

Fluoroscopic and roentgenologic examinations of his chest by Dr. Wm. Bryan showed zones of consolidation in the upper lobes of both lungs. There were multilocular cavities in the left upper lung in the anterior portion of the upper lobe in the subclavicular space. No fluid levels were seen in these cavities and the walls of the cavities were smooth in outline. The roentgenologic diagnosis was: bilateral upper lobar pneumonia; congenital cysts of the left upper lobe of the lung.

His course in the hospital was progressively downward. His temperature ranged from 99 to 104°, usually being about 102°. He became emaciated from 20 pounds 1 ounce to 17 pounds 10 ounces a few days before his death.

Signs of pneumonia (rales and impaired percussion note) persisted at both upper apices of the chest in front. On January 4, 1937, fluoroscopic and roentgenologic examinations revealed the right upper lobe still consolidated and markedly shrunken, but with the appearance of beginning resolution. The cystic areas of the left upper lung had the appearance of large emphy-

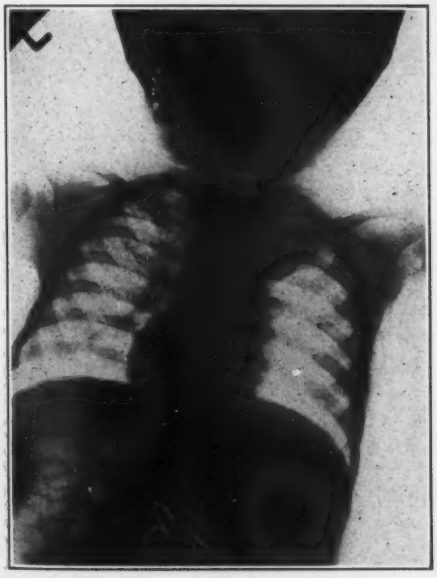

Fig. 2
Air expanding lung cyst.

Fig. 3
Air expanding lung cyst.

Fig. 4
X-ray of lungs removed at autopsy. Lung cysts have been inflated with an air pump. Air will enter, but will not escape.

sematous blebs. On January 12 it was noted that these cystic areas had become larger. Intratracheal injections of iodized oil were considered, but the patient's condition was so extremely bad that it was deferred, hoping that his pneumonia would show improvement.

At no time during his stay in the hospital did he show further signs of respiratory distress other than the usual signs of pneumonia. There was no marked cyanosis. He was not seen expectorating any large amount of fluid. There was no progressive dyspnea nor other signs that led us to believe that the respiratory system was being embarrassed by the cystic area's becoming larger. For these reasons no attempt was made to aspirate the cystic area. He died January 10, 1937.

The autopsy, performed by Dr. Warren Matthews ten hours after the death of the infant, revealed a large cyst measuring 8 x 6.5 x 6.5 cm. situated at the left upper lobe of the lung. It transmitted light readily and was filled with air. After the lungs were removed, the cyst was inflated readily with an air pump, but no air would escape.

This patient fits into the most plausible theory regarding congenital lung cysts. Cysts of varying sizes, existing from birth, may pass unrecognized until subjected to infection of the respiratory tract. Various other theories of origins have been advanced, such as that they are neoplastic,[3] that they are caused by congenital bronchiectasis, congenital atelectasis, lymph vessel dilatation, or congenital syphilis.[1]

Embryologically, formation of lung cysts readily can be explained. The bronchi develop as ramifications of entodermal tissue, becoming canalized almost immediately. Interference with canalization proximal to the termination of the ramification causes a portion of the radical to persist as a mass of cells. Canalization then begins again distal to the occlusion, producing a small canalized segment with mucous membrane, capable of secreting. This secretion accumulates and having no exit, forms a cyst. The rapidity of prenatal growth would depend upon the amount of secreting bronchial mucosa entrapped and the tensile strength of the walls of the cyst. Postnatal growth is more rapid than prenatal, being aided by negative intrathoracic pressure which begins with respiration. Infection is encouraged in the bacteria laden lung, playing an important part in the rupture and evacuation of the cyst. However, a few autopsies are reported in which no inflammation was present.

During a seizure of coughing the cyst may rupture into an adjoining bronchus, causing an

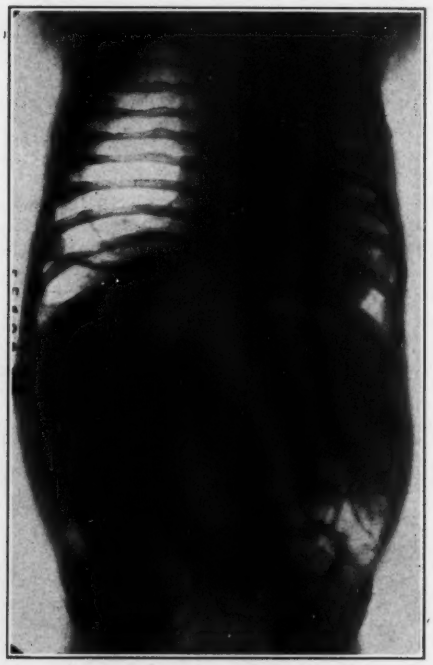

Fig. 5
Air expanding lung cyst.

Fig. 6
Air expanding lung cyst.

expectoration of its albuminous content. If a one-way valve is formed, preventing the egress of air, with each respiratory cycle the cyst may become larger in size. Increasing in size, with air under pressure, the cyst may displace the mediastinal contents and depress the diaphragm. Death may be due to decrease in the pulmonary field, as evidenced by progressive dyspnea and cyanosis.

In the second case, a white infant, one year of age, the cystic area occupied the entire right side of the thoracic cavity, the heart and mediastinal contents being markedly displaced to the right. On routine physical examination the signs in his chest were those of pneumonia, the diagnosis being made by roentgenological examination.

King and Harris report an instance in which one lung cyst occupied the greater portion of the thoracic cavity. Iodized oil was injected through the chest wall, and demonstrated on both sides of the mediastinum. Four years after complete recovery the iodized oil could be seen in only a small circumscribed area to the left of the mediastinum.

There is no group of symptoms characteristic of air expansile lung cysts. Usually the patient has had recurring attacks of respiratory infection. Cyanosis and dyspnea may be present. The child, in rare instances, may recover spontaneously. He may die during an acute attack, or most probably, die of pulmonary infection.

The diagnosis is made by roentgenological examinations, only one instance being cited in which a diagnosis of uncomplicated lung cyst was made. This is to be expected, since there is little in the symptomatology and physical changes on examining the chest: Large balloon cysts may be confused with pneumothorax and give the signs of bulging of the chest wall, limitation of motion, tympany on percussion, absent breath sounds and displacement of the mediastinum and diaphragm. Fluid cysts, prior to rupture and the entrance of air, should be suspected in atypical pneumonic processes, particularly those of protracted or recurring courses.

The prognosis of air expanding cysts is grave. Fluid cysts do not necessarily carry a serious outlook, but the development of infection or the establishment of bronchial communication are usually fatal complications. Of all types of congenital lung cysts reported since 1925, forty-six of 152 instances are under 3 years of age. Of the forty-six, thirty-six are dead. A record of cure is available of only seven of the remaining ten. An even higher percentage of deaths occurs in the first two years of life. In Koontz's series of 108 autopsies reported prior to 1925 of lung cysts of all types, twenty-seven occurred in patients under 1 year of age.

The weird clinical course, the character, location and extent of the cyst and the age and condition of the patient all present a difficult therapeutic problem. Thoracentesis has been employed successfully in a few instances. It may serve to prevent a fatal accident until more radical treatment can be used. Single aspirations are not only of little value, but may be harmful. Adams thinks a rubber tube with its end placed under water to equalize intrathoracic pressure should be attached to the needle. Iodized oil should be injected into the cysts at the thoracentesis for further study and observation.

Surgery will probably continue to reduce the high mortality rate in the future. The use of the thoracoscope, or straight cystoscope, and the cauterization of the aperture with sclerosing solutions seem to be the most logical approach. If the cyst involves an accessible part of the lung, lobectomy may be employed. With the high death rate, and the frequent occurrence during pulmonary infection, perhaps more surgery will be done in the face of infection.

When a fluid cyst is discovered, strict prophylaxis should be instituted. Respiratory infections should be prevented as far as possible, and when they occur, the child should be watched even more carefully than the ordinary pulmonary infection.

SUMMARY

The most probable theory of an air expanding lung cyst is that a congenital cyst, in the presence of pulmonary infection, enlarges rapidly. Occasionally it ruptures into an adjoining bronchiole. An air trap is formed, allowing air to enter but not escape. The death rate in this bizarre clinical picture is very high. Diagnosis is made almost entirely by roentgenologic examinations. Treatment in the past has been inadequate, depending on many factors, as the lack of resistance to infection and shock in the very young. Perhaps more surgery will be done

in the future even in the presence of pulmonary infection. Prophylaxis should be instituted in all known fluid cysts prior to the development of an air expanding lung cyst.

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DISCUSSION (*Abstract*)

Dr. James C. Overall, Nashville, Tenn.—In discussing any condition as rare as congenital lung cysts one must of necessity draw on the literature, as few doctors will have the opportunity of seeing even one case clinically. For of all the congenital cysts reported, only a few have been in infants and in still fewer was its course watched during life.

My experience with lung cysts has been limited to a congenital bronchogenic fluid cyst of the mediastinum, in a seven months old girl seen about a year ago. This case is being reported by the examining pathologist, Dr. Leland Johnson, in the *American Journal of Diseases of Children*.

This mediastinal cyst has apparently the same origin as the lung cysts, in that it is a misplaced bronchiole. It also has about the same symptoms and signs; hacking cough, usually non-productive, increased respiration, spells of cyanosis, and frequently difficulty in swallowing. In this seven months infant, the mediastinal cyst had caused so much pressure that the entire left lung and the upper part of the right lung were completely atelectatic, and had apparently been since birth. Thoracentesis had been attempted on two occasions by the referring physician, thinking the case one of empyema.

Most authorities seem fairly well agreed on the origin of these cysts; for in more than one case serial x-rays have been taken showing the cyst completely or partially filled with fluid, then later this entirely replaced by air. In the presence of an infection or violent coughing the cyst ruptures, the fluid drains out and the one-way valve-like opening remains allowing air to come in but not out. Now this origin suggests to me a form of treatment which I do not believe has been used and that is pneumothorax. It may not be practical, for the tensile strength of the cyst wall may not be great enough to allow the pressure to be increased sufficiently to collapse the wall of the cyst. If, however, it could be used it would certainly be less dangerous than thoracentesis. However, if the iodized oil used by Croswell and King is shown to have any definite effect in sclerosing or collapsing the cavity, it should be tried. In any condition in which the mortality rate is high, almost any treatment that is not too dangerous, yet offers help, will be tried. Of course, as Dr. Anderson mentioned, surgery of the lung is advancing so rapidly that it soon may offer a cure. It is important in the case of any bizarre and peculiar respiratory signs or symptoms to think of congenital lung cysts.

SYMPTOMS, DIAGNOSIS AND TREATMENT OF RENAL CYSTS*

By RALPH M. LECOMTE, M.D.
Washington, District of Columbia

A simple classification for renal cysts divides them into two main groups, parasitic and non-parasitic, using the term parasitic to denote infestation with animal parasites rather than infection by bacteria which are lower in the biologic scale and without a definite demonstrable life cycle. Parasitic cysts are caused by *Taenia echinococcus* or dog tape worm. Non-parasitic cysts may be divided into simple and polycystic, the former being subdivided into unilocular and multilocular. Dermoids and, at present, multilocular cysts are so rare as not to require separate consideration as a clinical problem, it being quite sufficient to include them with simple cysts, while the small multiple retention or nephritic cysts, noted only on exposure of the organ, have no practical clinical or surgical significance.

HYDATID CYSTS

The low incidence of renal hydatids both in this disease (2.45 per cent)[1] and in North America (twenty-five cases found reported to October, 1934) make it unnecessary to go into detail regarding it. However, since an occasional case is encountered the essentials should be understood by those who do renal surgery.

As we have had no personal case, our description is taken from the literature, in particular from Craig and Lee-Brown.[2] They are classified as closed and open, depending on whether the cyst communicates with the pelvio-calyceal system of the kidney or not. As long as they remain closed, they may give no symptoms except those due to their weight or, if they are large enough, by the lumbar mass that they occasion. After they have become open, hematuria and renal colic occur and pieces of chitinous membrane, described as resembling grape skins, may be noted in the voided urine. Unless the disease is suspected and demonstrated by finding hooklets in the urine or by a positive allergic skin reaction, the preoperative diagnosis is apt to be that of neoplasm or pyelonephritis and treatment carried out accordingly. If the disease is recognized while it is still closed and the kidney is

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not badly damaged, marsupialization may be practiced. The cyst is exposed by as small an incision as practicable, its contents are carefully evacuated, the interior treated with alcohol which is then removed and the cyst wall stitched to the deep layer of the abdominal muscles. The abdominal wall is then closed with a small rubber drain carried down to but not into the cyst. Desiderata of the operation are to evacuate the contents completely, to avoid soiling the surrounding tissues with the cyst contents, lest extension of the disease occur, and to prevent the entrance of bacteria into the cyst, for fear that a fatal infection may result. For these reasons a two-stage operation, first stitching the cyst wall to the abdominal wall and opening and treating it only after adhesions have developed, may be advisable.

Nephrectomy is desirable in dealing with open hydatids, but may be impracticable because of the size of the cyst and extensive adhesions to near-by organs. In that instance the method of marsupialization described above may have to be practiced.

SIMPLE CYSTS (SOLITARY)

Our knowledge of solitary cysts may be briefly summarized by stating that they are uncertain as to etiology, indefinite as to diagnosis and favorable as to prognosis. The circumstances under which they are recognized vary greatly for unless the weight is sufficient to drag on the kidney and produce lumbar pain, or the volume great enough to produce a palpable mass, cyst is not apt to be suspected, and thus it is not likely to be searched for and recognized. Perhaps most solitary cysts are found because of the occurrence of some renal accident or abdominal complication which leads to an examination sufficiently thorough to show them up. They are often not suspected at all and are disclosed only at operation for some other disorder, usually renal in type.

A definite diagnosis ordinarily rests on the demonstration of one or more of the pyelographic evidences of renal neoplasm. These are incident to the intrarenal portion of the cyst which may either pull upon or elongate one or more of the component parts of the renal pelvis (calyces or true pelvis) or encroach upon them, causing narrowing, deformity or obliteration with possibly secondary dilatation in the parts above. They may also be due to the volume of the cystic mass which may displace the kidney pelvis, and the kidney as well, in various directions or distort the ureter so that its relations either to itself or to other organs are changed (angulation; displacement, Braasch, Urography, 1929, page 307). The other classical clinical signs of neoplasm, massive hematuria and lumbar pain may or may not be present. A combination such as this demands exploration lest a neoplasm be present and develop unhindered and, at operation, a cyst instead of a tumor may be found. At other times cysts are noted as an incidental finding in operations for traumatized kidneys, hydronephroses, stones, neoplasms and infections, tuberculous or non-tuberculous.

Our interest is mainly centered on what should be done with a cyst when it is encountered either as a planned operative procedure or unexpectedly at operation for some other condition. As a pathologic process, solitary cysts fall into two classes, serous cysts with clear fluid contents and hemorrhagic ones the contents of which present more or less fresh or old blood. With regard to the former, the simplest procedure is to open the cyst, trim the wall down to the line of the renal parenchyma and destroy the remaining lining membrane with carbolic acid followed by alcohol and then closing it without drainage.[3] Other methods consist of peeling the cyst from the kidney or excision of the cyst along with a wedge-shaped piece of kidney tissue. If this is found to be impracticable either because of the hemorrhage that occurs or because the kidney itself is so badly damaged that conservation seems unwise, nephrectomy may have to be done. Such a situation may readily arise if the cyst is situated in the middle portion of the organ. If nephrectomy is unusually hazardous because of technical difficulties, as much of the cyst wall as convenient may be removed, its internal secreting surface destroyed by carbolic acid, as noted above, and the opening stitched to the abdominal wound; this may give a fairly satisfactory result, but the hazard of a permanent draining fistula must always be considered and the procedure avoided if possible.

If the fluid content of the cyst is bloody, we feel nephrectomy should be done, for, of the 42 cases found recorded in the literature by one of us,[4] 13 were found to have frankly neoplastic tissue in their walls. Our own experience in examining the wall of a hemorrhagic cyst and of finding neoplastic elements only after prolonged search,[5] leads us to believe that the many hemorrhagic cysts either have their origin in or are associated with malignant neoplasms of the kidney and that, if a sufficiently long and thorough search were to be made, a larger proportion than have

been reported might be found to have contained malignant elements in their walls. Certain exceptions to this rule may be made[6] if no macroscopic evidence of malignancy is found on careful examination of the cyst wall. If, however, the wall is unusually thick or presents thickened areas or if the lining membrane is at all rough or shaggy, even in part, malignancy may be suspected and nephrectomy carried out.

It is noteworthy that in at least two of the cases reported[7] neoplasm of the kidney occurred at a site remote from that of the cyst. Ezickson and Greene have recently reported the case of a cyst containing muddy serous fluid that was enucleated, and which was later shown to be an adenocarcinoma.

POLYCYSTIC KIDNEY

With regard to polycystic kidney, the data given for solitary cysts are reversed; the etiology instead of being uncertain is almost always and almost surely congenital, the diagnosis instead of being indefinite is generally quite certain, and the prognosis instead of being favorable is poor.

The condition has long been recognized as having a congenital background. Of the theories that have been advanced from time to time to account for the condition, that of Kampmeier,[9] which has the merit of having been demonstrated, at least in part, in fetal kidneys and which gives a logical explanation for the occurrence of solitary cysts, seems to be quite satisfactory for polycystic kidney as well. Generally, we believe, the disease is congenital and bilateral, but the specimen from one of our patients indicates that at times it may be unilateral and arise from repeated or prolonged attacks of inflammation, thus justifying the theory of papillitis advanced by Virchow.[10]

Our present fashion of looking on those kidney lesions in which the advisability of surgery is considered dubious or contraindicated, as medical, and those that are susceptible of improvement or cure by surgery as urological, permits us to group the presenting symptoms of polycystic kidney as either medical or urologic.

In the medical group, the symptoms are often those of contracted kidney, and may present any of the wide variations with different organ system manifestations that that syndrome may exhibit. Generally there is hypertension and lowered renal function, and, if, in addition, palpable lumbar or renal masses are present, the possibility of polycystic disease is brought to mind. In those of the urologic type, hematuria, pyuria, or bladder symptoms or lumbar pain may bring the patient to the physician and, in some instances, the pain, palpable mass and hematuria are so marked as to make one suspect neoplasm.

Often in the medical type the symptoms and physical signs noted above, coupled with the history, are sufficient to make the diagnosis certain, but, if reasonable doubt exists, urography can be utilized for confirmation. All of these signs may, however, fail and the true state of affairs be revealed only after time enough has elapsed for diagnostic signs to develop. Urologic types will each present the symptomatology of the particular disease or complication that is present and it should be kept in mind that, while the polycystic kidney may be the basic lesion, any other sort of kidney disease may be engrafted upon it. In many instances urography, either intravenous or instrumental, will give sufficiently definite diagnostic evidence of the disease. The pyelographic changes are easier to recognize than to reduce to precise description. They consist of alterations due to compression of the various parts of the pelvis either by the individual cysts or the conglomerate masses. In the earlier stages they consist mainly of a peculiar crescentic distortion of the terminal parts of the minor calyces due to elongation of the niches about the papilla. These are often spoken of as "discoid" or "biscuit cutter shaped" minor calyces. In advanced cases the pictures often simulate closely those seen in renal neoplasm.[11]

The disease may also be suspected if a rather large kidney pelvis spread out over a space larger than the usual kidney area is present.

The prognosis is poor, but a relatively long and reasonably comfortable span of life may be obtained under certain circumstances which cannot, unfortunately, be either outlined or controlled with exactitude

Those exhibiting only medical symptoms, the nephritic or hypertensive cases, require symptomatic treatment which is, ordinarily, of a strictly medical nature. Surgical procedures such as puncture of the cysts, decapsulation, and so on, have been done, but apparently without influencing the progressive cyst formation or the squeezing out of the functioning urinary tubules more than temporarily, at most. Puncture of the cysts may have a beneficial effect on the symptoms, both general and local, and the tendency now is to operate upon cases in which for a long time a conservative attitude has been observed. Inflammation, neoplasms, ruptures, stones, and obstructive lesions of various types do not differ greatly either in their pathology or clinical effects from those occurring in the congenitally

normal kidney and their treatment need not be changed materially. If nephrectomy is contemplated, and the need for it may arise unexpectedly in almost any renal operation, one should be assured of a sufficient functional reserve in the kidney that may have to be left behind. The fact that the remaining kidney may progressively enlarge and finally fail, need not be a detriment to the removal of the polycystic kidney which, in addition, presents a disease which is hazardous to the life or health of the patient. It is true that the remaining polycystic kidney will not be improved by the removal of its similarly affected fellow, but, if the general and renal condition of the patient demands it, the polycystic kidney that is otherwise diseased should be removed for the same reasons that a congenitally normal one would be, and with the same precautions as to the prevention of renal insufficiency and death from anuria. On the other hand, a polycystic kidney should not be removed because of its polycystic condition alone.

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DISCUSSION (*Abstract*)

Dr. J. Ullman Reaves, Mobile, Ala.—In 1923 I toured South America with the American College of Surgeons. This gave me an opportunity to have a first hand view of the hydatid cysts as handled in the Argentine by the several hospital staffs of Buenos Aires. I attended the clinic of Dr. M. Herrera Vegas, who in one of his papers tabulated 560 cases of hydatid cysts in which the kidney ranked third in the order in which the different organs were attacked, and at that only 13 of the total number of hydatid cysts appeared in the kidney. The echinococcus embryo, upon reaching the human intestine, has its outer covering digested away, thus freeing it to be carried through the portal system to the liver, where most hydatid cysts are found. Extension further is either by embryos which fail to lodge in the liver structure or are metastatic from those which do sojourn in the liver and produce hydatid cysts.

This disease is not easily recognized, even in the Argentine. In every "set-up" in the operating room, a suction apparatus was made ready for use. On asking why this was so, I was told that regardless of the preoperative diagnosis, hydatid cysts, because of their prevalence, size, and location, could and did cause symptoms simulating many other surgical conditions, and upon operation might be found in any given case.

A statement by Greenberg, Brodney and Robbins, in 1934, that pneumoradiography was to be avoided in cysts of the kidney because of the danger of puncturing the cyst with the accompanying possibility of dangerous complications, was certainly not in the mind of Carelli of Buenos Aires, for I saw him make several kidney pictures after his technic of injecting 125 c. c. of oxygen into the perirenal fat. These roentgenograms were clear cut and diagnostic, causing me to wonder since why this method is not extensively used in this country.

To quote from Deve, "When the embryo reaches the organ in question, the formation of the adventitious cyst is commenced by local action set up by the connective, vascular and migratory elements of the tissues. The parenchymatous cells are at first disintegrated by a toxic necrosis, and later they disappear through mechanical pressure. The mechanical lesions, or eccentric fibrous atrophy, caused by the progressive expansion of the hydatid vesicle are more extensive than those produced by the toxic effects due to the presence of the hydatid. The peripheral veins and arterioles disappear, obliterated by mechanical pressure, thus rendering the adventitious wall of the cyst avascular."

This, to my mind, answers the divergent opinions of both Hepler, who, after very careful experiments, advanced the theory of infarcts and tubular obstruction as factors producing solitary cysts of the kidney, and of Latteri, who implanted fragments of the mucosa of the ureter or renal pelvis into the kidney parenchyma to produce solitary cysts. Both of these gentlemen are undoubtedly correct, but Deve pointed out that conditions simulating each of these experimenters' work caused hydatid cysts either singly or collectively, and I rather believe that this is true of all kidney solitary cysts.

Dr. LeComte calls our attention to the fact that solitary cysts were not often suspected, being disclosed at operation for some other disorder, usually renal in type. But should these cysts begin to produce symptoms and the patient come in for a urological survey, it should be determined whether the tumor is cystic or solid. Pelvic deformity is not so extensive if we are dealing with a cyst as it would be with a neoplasm of like dimensions and location, unless it be a very small cyst. Cysts occasionally cause rotation or deviation of the axis of the kidney. In this day of perfected soft tissue technic we find a distinct difference in the manner in which cystic and solid tumors record themselves, due to the variation in scattering behavior of the x-ray beam when passing through liquids and solids. Thus in cystic tumors we will find the outline of the kidney or psoas muscle, or both, recorded on the x-ray film through the shadow of the tumor, as well as the outline of the shadow of the cyst itself adjacent to the renal shadow and with density in marked contrast to that of the kidney, psoas muscle, or both as the case may be. Solid tumors completely obliterate these shadows if they overlie them, due to their density. This is

a very important point, allowing us to go ahead in the case of a cyst or do preoperative radiation in the case of a solid tumor should we so elect.

During the past decade urologists have given considerable study to cysts of the kidney, and we may expect earlier diagnosis in these cases should we evaluate in the light of present day knowledge and past experience. It is generally believed today that polycystic disease is congenital and some authors suggest sterilization of these patients as a means of its eradication, but this brings us up against an awful handicap when Oppenheimer brings out in his monograph that the average age of these patients at the time of onset of symptoms is 41.5 years, and if we are to go far in eradication of polycystic disease by sterilization of the patients, we must diagnose these cases much earlier than we are doing at present.

Dr. LeComte says that the prognosis in cases of polycystic disease is poor, therefore we must remove all foci of infection, and see that the patient lives a life of regular habits. These patients learn before they present themselves that they must do all things in moderation except drink water and rest, and when the time comes that surgical procedures are indicated we shall find our prognosis as favorable as the patient's reserve has been stored up and conserved.

Diagnosis may be arrived at much earlier in cases of polycystic disease if we combine intravenous with retrograde urography. The cystoscope is passed and the pelvis of the kidney injected after time enough has elapsed since the intravenous injection to allow the functioning kidney parenchymatous tissue to become engorged with the process of eliminating the opaque medium. This serves to bring out the shadow around the cysts more clearly.

Dr. Eugene R. Whitmore, Washington, D. C.—As Dr. LeComte has told you, this study of renal cysts is a joint work, and my part will be presented in the Section on Pathology tomorrow. I want to testify to the great pleasure I have had in carrying on the work with Dr. LeComte; and I consider it very important that the pathologist carry on work with clinicians at every opportunity.

It is of importance that there are foci of echinococcus infestation in the United States, and that apparently the cycle has been established in the moose and the wolf in some places in Minnesota. This, with the ready travel between various countries, makes it necessary for the surgeon to be on the lookout for hydatid cysts: it is very easy to make the intracutaneous test in any suspicious case; and it is advisable to be ready for an unexpected hydatid cyst, as is regularly done in Argentina.

Dr. LeComte's hemorrhagic cyst of the kidney led us to look up the reported cases of hemorrhagic cyst of the kidney, and we found that, after ruling out reports of hemorrhage into a kidney tumor, in almost one-third of the cases reported as hemorrhagic cyst of the kidney the pathologist's report stated that tumor cells were found in the wall of the cyst. This point is of practical importance: especially in thick-walled hemorrhagic cysts, one must be sure there are no tumor cells in the wall, as the presence or absence of tumor cells will determine the nature of the operation to a great extent.

Polycystic kidney is a very interesting subject. Kampmeier's theory of the origin of polycystic kidney is probably the most widely accepted; though we have the theory of failure of connection of the collecting tubules with the connecting tubules; and the older theory of the French and Italian authors of tumor. The heredity, and the associated malformations, are very interesting features of polycystic kidney. The urologist sees these cases first, but the pathologist finally gets them.

Dr. LeComte (closing).—Dr. Reeves has brought out a point that is new to me and which I think may be important: that is the fact that solid tumors may obliterate the underlying shadows of the psoas and other tissues, while cysts, being of lesser density, will not obliterate them. His explanation of the formation of hydatid cysts is also interesting.

If anything has come to me from the study that Dr. Whitmore and I have made, it is a conviction that it is not possible to differentiate clinically between neoplasm and cyst, and that one may mimic the other in every respect. If a cyst and a hypernephroid growth are found at operation, it is usually impossible to determine which of the two was primary although, of course, the neoplasm may be the dominant pathologic condition at operation.

URINARY FINDINGS IN THE NEW BORN*

REPORT OF THREE CASES OF NEONATAL NEPHRITIS

By CHARLES E. CONRAD, M.D.
Harrisonburg, Virginia

Having been interested in pyuria of the new born since 1926, when I reported three cases, I decided to examine the urine in a group of new born infants, using consecutive births at the Rockingham Memorial Hospital.

The following is a report of this work with the addition of three cases classed as congenital neonatal nephritis, which occurred during the summer of 1937.

Craig reported recently 61 cases with urinary infections, using healthy children as controls.

In our work, we felt that examination of infants of 190 consecutive births would give some knowledge of expectancy of pyuria in the average birth.

All specimens of urine were obtained during the first 3 days of life: fifty per cent during the first 24 hours, 40 per cent during the first 48 hours, and 10 per cent during the first 72 hours. Specimens from a portion of the girl babies were catheterized; from the remaining babies specimens were obtained by fastening on a sterile glass tube with adhesive plaster. All specimens were examined soon after they were voided.

Urinary findings as to albumin, pus and casts,

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with analysis and discussion of symptoms, follow:

	Albumin
145 cases	None
17 cases	Trace
20 cases	Two plus
8 cases	Four plus

Pus was estimated by placing a drop of urine on a slide and covering it with a coverglass, then examining it under a high power lens (4 mm. 0.65).

	Pus
151 cases	None or an occasional cell
15 cases	Ten to 20 cells per high power field
15 cases	Twenty to 60 cells per high power field
9 cases	Over 100 cells

All cases were examined again when 10 days old. Twenty-three cases continued to show pus. In those with over 100 cells, 3 cases had fever, 2 showed muscular twitching, and 1 case had attacks of cyanosis and nursed poorly.

Casts.—Four cases showed hyalin casts; and 6 cases hyalin and granular casts.

Temperature.—Sixteen cases had fever with pus; 23 cases had pus with no fever; and 12 cases had fever with no pus.

In the 16 cases with fever and pus, the fever was of an irregular type. Eleven cases had maximum temperatures of 100 to 103°; 5 cases had a maximum temperature of 103 to 104.5°.

Of the 9 cases with 100 or more pus cells, only 3 had fever. The cause of fever in cases with no pus was as follows: Five patients had inflamed ears; 1 was dehydrated; 2 had cerebral hemorrhages; and in 4 the cause was unknown.

Vomiting.—Three cases with severe vomiting had pus. Four cases had severe vomiting without pus. One case had pyloric stenosis, was operated upon and recovered. Two cases had cerebral hemorrhages.

Cases with occasional vomiting are not classified.

Cyanosis.—Three cases occurred with pus (no other reason found to account for it). Two cases had cerebral hemorrhages.

In 4 cases the infants with pus were very fretful.

Eight cases with pus either refused to nurse for the first two days, or nursed a very little after great effort on the part of the nurse. Four other cases without pus came in this group of infants who nursed poorly: two cases with cerebral hemorrhages, 1 case with inflamed ears, and 1 case without definite cause.

Convulsions.—In a case with innumerable pus cells, the baby did not void for 30 hours, then 30 c. c. of urine were obtained by catheterization. One case had 4 plus albumin; 1 had 3 plus albumin and casts, and the mother had 4 plus albumin; and 1 case had cerebral hemorrhage.

Fourteen cases were examined at the end of two years. Of these, 13 cases showed no pus in the urine, and 1 continued to show pus at irregular intervals. In this group were 8 of the 9 cases showing over 100 cells. The other 21 cases I was unable to re-examine.

Urine Examination of the Mothers.—Two mothers had 4 plus albumin, casts, and red blood cells. The babies were normal.

Four mothers had albumin and numerous pus cells, babies normal.

Two mothers had 4 plus albumin, casts, and red blood cells; both babies showed 3 plus albumin, casts, and red blood cells, and one baby had convulsions.

The urine was negative in other mothers of babies comprising the 190 cases reported.

Treatment.—Sodium citrate was used to alkalinize the urine; each dose was given in one ounce of water. In a few cases when the desired amount of water could not be given, 60 c. c. of Hartman's solution were given as a clysis once or twice a day. Those who showed nervous symptoms were given phenobarbital or sodium bromide.

DISCUSSION

From the foregoing statistics you will see that out of 190 consecutive births, 39 showed pus in the urine during the first three days of life. Of these, about one-third (12) had recovered by the tenth day. At the end of two years, the urine of 14 of the above cases was examined. It was found that 13 of the cases had urine free from pus and only one continued to show pus. Of the cases with pus, 16 had fever and 23 did not have any fever. Eight of the 14 cases examined after two years were in the group showing over 100 cells at birth.

The maximum point of temperature in the different cases ranged from 100 to 104.5°. Strange to say, only 3 of the cases with over 100 cells per field showed a temperature rise.

Three cases showed definite cyanosis.

Four cases were very fretful.

Eight cases nursed very poorly.

One case with pus had convulsions; this is the patient who did not void for the first 30 hours, and then was catheterized.

Two other cases had convulsions with a large amount of albumin, but no pus. The mother of one of the last two cases had a large amount of albumin and casts in her urine when the baby was born.

Three cases, in addition to the one with convulsions, voided very small amounts for three days. One of them voided in small amounts for two days, then went 34 hours without voiding; after that, in only small amounts for three more days.

A number of the mothers were brought to the hospital from outlying districts, with no prenatal care, and only after complications developed were they brought in. In this group were the following:

MATERNAL COMPLICATIONS

Two mothers with 4 plus albumin, casts, and red blood cells.

Four mothers had 4 plus albumin and numerous pus cells; all six babies of these mothers had normal urinary findings.

Two mothers had 4 plus albumin, casts, and red blood cells; and both their babies showed 3 plus albumin, casts, and red blood cells, but no pus.

This shows only 2 babies out of the 8 in the above group affected. It will be noted that pus in the urine of the mothers had no effect on the babies; in the 3 cases which I reported in 1926 two of the mothers had pus in the urine.

SUMMARY OF FINDINGS IN SERIES OF NEW BORN INFANTS

Total number examined	190
Number showing pus during first 3 days	39
Pus in urine on tenth day	27
Total number showing symptoms	19
Fever	16
Nursed poorly	8
Very fretful	4
Cyanosis	3
Partial anuria	3
Convulsions	1
Fourteen of above cases examined at age of 2 years. Number showing pus	1

SUMMARY

You will see from the table that about one in five of the total cases examined showed pus in the urine. Of the 39 cases showing pus, only 19 manifested symptoms, or one in ten of the total number examined.

The leading symptom, which was fever, occurred in 16 cases. The next symptom in frequency comes under the heading "nursed poorly," with 8 cases. In the next group, "very fretful," were 4 cases. Then cyanosis and "partial anuria," with 3 cases each. Convulsions occurred in one case.

The above findings I feel give sufficient data to emphasize the importance of routine urine examination in the new born.

THREE CASES CLASSED AS NEONATAL NEPHRITIS

Case 1.—Baby H. was born normally at 9:00 a. m. April 15, 1937. She was slightly cyanotic and cried very little at birth; but her color improved in a short time. At 1:00 p. m. she became cyanotic again, and had several slight convulsions, breathing irregularly. She was given caffeine ¾ grain, oxygen inhalation, and 5 grains of sodium bromide. She remained cyanotic with some muscular twitching until 5:30, at which time she became very cyanotic, and respiration practically ceased. At 6:00 o'clock, I saw the baby for the first time, and ordered for her a heart stimulant given every 3 hours, 10 grains of sodium bromide every 3 hours and 5 c. c. of 10 per cent calcium gluconate intravenously. My examination revealed a very cyanotic baby with respiration superficial and rapid. She showed internal squint with marked lateral nystagmus; the arms were flexed and rigid, legs extended and rigid, there was marked generalized edema of the body, extremities and face. Her condition remained much the same until the following morning, when her color seemed better.

Urinalysis on the morning of April 16 showed an acid reaction, 2 plus albumin, 5 to 7 red blood cells, loaded with pus cells, and 14 to 18 granular casts. In the afternoon she was given 60 c. c. of Hartman's solution by hypodermoclysis. Cyanosis was better, and convulsions were not so frequent. Sixty c. c. of Hartman's solution were given again at 11:30 p. m. She vomited at times during the day, and this increased during the night.

April 17, we started sodium citrate every 4 hours. The baby's general condition remained about the same, with attacks of cyanosis. Convulsions were less marked and she showed muscular relaxation at intervals. Urine today contained 3 plus albumin, 1 to 3 red blood cells and 3 to 6 pus cells.

On April 18, she was given a clysis of 60 c. c. of Hartman's solution. She appeared quiet during the preceding night. Her general condition seemed somewhat better all day, with definite improvement in edema.

On April 19, the urine showed 3 plus albumin, 8 to 10 red blood cells, and a few coarse granular casts. All medicine was discontinued except sodium citrate and one hypodermoclysis of 60 c. c. of Hartman's solution. Convulsions became worse again at 5:00 o'clock this afternoon.

On April 20, the baby had been cyanotic since early the previous night, and convulsions and spasticity had returned. Sodium bromide and the heart stimulant (pyridine beta carbonic acid diethylamide) were started again. Oxygen was given continuously. Urine examination today showed 2 plus albumin, a few coarsely granular casts, 6 to 8 red blood cells, 4 pus cells. Generalized edema had become worse. Five c. c. of 10 per

cent solution of magnesium sulphate intramuscularly, every 6 hours, were ordered.

Her condition remained very much the same until 3:30 a. m. April 22, at which time she died.

A Kahn test was done on the blood and reported negative.

Autopsy was refused.

Case 2.—Baby S. was born normally on April 27, 1937, at 1:00 a. m. He had a convulsion at 3:00 o'clock, with definite nervous manifestations and twitching during the night and the following day. He was very cyanotic at 9:00 a. m. He was seen first by me at 1:00 p. m., at which time he showed generalized edema, was quite cyanotic, showed muscular twitching of the arms and legs, and the superficial reflexes were exaggerated. Urinalysis today showed: acid reaction, albumin 2 plus, many fine and coarse granular casts, 5 to 6 red cells, 6 to 8 white blood cells to a field. The child was given 3 grains of sodium citrate and 1/6 grain sodium phenobarbital every three hours. At 2:30 p. m. he had mild convulsive seizures. He was given 5 c. c. of 10 per cent solution of magnesium sulphate, every 8 hours, for 3 doses. He had slight difficulty in swallowing. His rectal temperature was 96 to 97°.

On April 28, the baby showed some improvement, but still had mild muscular jerking with slight cyanosis. Urine examination was 2 plus albumin, 4 fine granular casts, occasional red blood cells, and 2 to 4 white blood cells.

April 30, his rectal temperature rose to 98.8°. The general condition was definitely improved. There was very little edema. Urinalysis showed albumin 2 plus, 2 to 4 red blood cells, an occasional granular cast and an occasional white blood cell.

On May 4 he continued to improve, nursing well. Urine examination showed 1 plus albumin, a rare granular cast, 3 to 6 red blood cells, and 6 to 8 white blood cells. Phenobarbital was discontinued. There was no edema.

On May 13, the child was discharged in good condition. Urinalysis showed no albumin, no casts, and no red blood cells. The child was not weighed for the first two days. On the third day he weighed 5 pounds 13½ ounces. On the fourth day he weighed 5 pounds 11½ ounces. On discharge he weighed 6 pounds 1 ounce.

I regret that he was not weighed on the date of birth, as there appeared to be a very definite loss of weight, due to loss of edema, during the first four days.

Case 3.—V., a baby boy, was born normally at 7:00 p. m. April 20, 1937. His weight was 7 pounds and 14½ ounces. He cried a great deal with a rather shrill cry. A history note says he was very nervous on April 21 and 22. I saw him first on April 23, at which time he was somewhat cyanotic with definite mild convulsions affecting all the extremities, and moderate generalized edema. A specimen of urine sent to the laboratory showed: albumin 3 plus, acid reaction, 15 to 20 red blood cells, a few hyalin casts, and it was loaded with pus cells. His temperature was 98.6°. The nurse said that he was edematous from birth.

On April 24, his condition was about the same. He was given phenobarbital and sodium citrate. Urinalysis showed: three plus albumin, 15 to 20 red blood cells, 20 to 30 pus cells. The temperature was 98.6°.

On April 26, the baby was quite drowsy, and all nervous symptoms were very definitely improved. Urine examination showed albumin 1 plus, an occasional red blood cell, 8 to 10 pus cells, and no casts.

On April 28, the baby had shown no cyanosis for the preceding 48 hours, and he had been nursing well at the breast. All nervous symptoms had disappeared as well as the edema. Urine examination showed no albumin, alkaline reaction, an occasional red blood cell, 10 to 12 pus cells, and no casts.

On April 30, the baby appeared normal in every respect. His weight was 8 pounds and 1 ounce. Urine examination showed alkaline reaction, a trace of albumin, no red blood cells, no casts, only an occasional leukocyte. He was discharged, recovered.

On May 26, his weight was 10 pounds 2 ounces. Urinalysis showed: acid reaction, no albumin, no red blood cells, 8 to 10 pus cells, and no casts.

Craig, in his paper, "Urinary Disorder in Neonatal Period," mentions twelve cases with edema, but, if I interpret correctly his cases, they were different from the three here reported, in that his cases showed localized edema which became more general in the severe case, while these cases showed a generalized edema at birth.

These three cases were all normal births, showing generalized edema at birth. They were all cyanotic at times and had convulsions. The urine in all contained albumin, red blood cells, casts, and two had pus. All three mothers had normal antipartum histories.

We have seen a few cases with edema appearing several days after birth; also cases with localized edema at birth, but they were different from this group.

Two recovered and one died. It was my pleasure that Dr. M. Jay Arena saw all three of these cases with me, and I am happy that he is here today to discuss them.

I wish to thank the attending physicians at the Rockingham Memorial Hospital for allowing me to examine these cases, and also to thank Miss Shaw, Mrs. Hering and others for their help in examining all urine specimens.

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DISCUSSION (*Abstract*)

Dr. Harold T. Nesbit, Dallas, Tex.—Studies of neonatal urine were reported almost a century ago. The first appeared in 1841 by Charceley, who noted albuminuria at necropsy in sixteen new borns. His work was confirmed by Prout and many others during the following year. A controversy then existed as to whether this albumin was due, or not, to postmortem pathological or physiological changes. This feud apparently died a natural death and not until years later was any particular interest manifested in the subject in medical lit-

erature. Near the beginning of this century, Escherich and Finkelstein, V. Reuss, and Ewald reported studies of neonatal urine in small groups of cases. Dorhm first examined urine obtained by catheterization directly after birth.

Ewald in Germany found albuminuria in 87 per cent of infants on the first day, 100 per cent on the third day, 50 per cent on the eighth day, and only in isolated cases during the second month. Parrot and Robin of the French school, however, found albumin only in exceptional cases. Heated discussion followed between the German and French students regarding the discrepancy of their findings, which was never settled. They arbitrated by saying that the variance must depend on racial characteristics (whereas it was probably due to different technics).

Again, a quarter of a century elapsed before the interest in neonatal urines was renewed. Dr. Conrad should be given credit for the revival of these studies. After his report of three cases of neonatal nephritis in 1926, treatises by Helmholz, Sauer and others appeared in the literature. An excellent paper on this subject was read at this same session just ten years ago by Dr. David Greer.

Of the larger series, the presence of neonatal albumin has varied from a low 27.7 per cent of Greer to 100 per cent (Ewald, Flensberg). Albuminuria was observed by Conrad in 38 per cent.

Opinions as to the influence of labor vary considerably. Ewald and V. Jaschke report that the offspring of prolonged labor showed albuminuria more frequently. These studies were not confirmed by Heller, Franz and V. Reuss. However, the difference of only 69 and 76 per cent between the normal and prolonged labors would, it seems, be within the limits of error. Dorhm, Ewald and V. Reuss state that birth trauma produces albuminuria rather constantly, which is severe and lasts for months. Greer found neonatal albumin with no greater frequency after birth trauma or in cases of nephritic and eclamptic mothers. "Lordotic stretching" of the newly born (Jehle), metabolic disturbances (Martin and Ruge) and acidosis have, without support, been given as causative factors. Although there have been many theories regarding the pathogenesis of neonatal pus and albuminuria, the plausible one (of low fluid intake and anhydremia) was advanced by Czerny. On this basis, he argued, the urinary findings are due to drying and therefore should be classed as exsiccosis albuminuria. Czerny's theory, now supported by animal experimentation, is upheld by Helmholz, Amberg, Campbell and most present day observers. Anatomically, there occurs a cloudy swelling of the tubules which does no permanent damage and is of little clinical significance. In his new monograph, Campbell says that normal urine during the first few days of life would be considered distinctly abnormal in older infants. It is scant (15-150 c. c.), highly concentrated, usually contains albumin, red cells, pus, and casts. These usual findings are due to anuria. He says that this is physiological in the new born, of no concern if the infant is normal otherwise, and disappears with the ingestion of large amounts of fluids.

Without more searching investigation, the cases reported today cannot be described as cases of renal impairment. They evidence cyanosis, tonic and clonic spasm of the extremities, convulsions, spasticity, exaggerated reflexes, shrill cry and generalized edema. These symptoms closely parallel those of neonatal tetany as reported by Sahannon and others. The generalized edema occurring in tetany could produce a cloudy swelling of the tubules and therefore an exsiccosis albuminuria. As is true with tetany, the administration of calcium and phenobarbital produced a most favorable response in Dr. Conrad's cases. At any rate I think it is advisable to be cautious in making a definite diagnosis of nephritis without further studies.

In future analyses of neonatal urine, a tabulation of the concentration, ketone bodies and bacteria would create a better understanding. Without urine culture it is a bit arbitrary to establish a diagnosis of urinary infection. Where clinical symptoms are present, blood chemistry, and, where feasible, necropsy reports should be made to establish neonatal nephritis as a definite diagnosis. An authoritative paper on this subject was published by Hurt in 1929. He found 5 per cent urinary tract abnormalities in postmortems of newly born. This is a point to be kept in mind, particularly when considering nephritis of the new born.

Dr. Conrad's presentation launches anew the historic controversy as to whether the high percentage of neonatal albuminuria is of pathological or physiological significance. His paper will, I hope, stimulate further studies and discussion of this fascinating subject. I shall henceforth make more detailed urinary studies on the newly borns, endeavoring to corroborate his belief that fretful, cyanotic, feverish new borns, or babies refusing to nurse or who experience convulsions, may have a neonatal nephritis.

Dr. Jay M. Arena, Durkam, N. C.—I was fortunate in seeing Dr. Conrad's patients with neonatal nephritis and in being able to follow them for a short time. What interested me most, of course, was the origin of the nephritis. As can be seen from Dr. Conrad's excellent report, everything possible was done to establish the etiology.

Although the subject of nephritis has been studied from many aspects, comparatively few reports are to be found on the manifestations of the disease in infancy. Jacobi emphasized the intestinal and toxic origin of neonatal nephritis, but this explanation is unlikely here, since the mothers showed no toxic manifestations, nor did the infants show any signs of an infection that might have caused severe nephritis in the first few days of life. The few cases reported in the literature showed a very high mortality and it was gratifying to hear of the outcome of Dr. Conrad's patients. I was interested, also, in the two-year follow-up of the 14 cases of pyuria in the new born. Only one of the 14 cases still showed signs of pyuria. Recently, Wharton, Gray and Guild reported a series of thirty girls and young women who were examined, on the average, 10 years after the last attack of pyuria. Only two were in poor health, and the other 28 had no complaints whatever. However, urologic examinations showed that 17 or 57 per cent had definite abnormalities in the urinary tract.

Dr. Conrad (closing).—I think the fact that the generalized edema in the three cases reported existed at birth is against the explanation suggested by Dr. Nesbit, that they be classed as neonatal tetany. Dr. Nesbit says that the three cases I reported in 1926 were neonatal nephritis. In this he is mistaken, as the title of the paper was "Congenitally Acquired Pyelitis."

ROENTGENOLOGICAL TREATMENT OF VARIOUS BLOOD DYSCRASIAS*

By JAMES J. CLARK, M.D.
Atlanta, Georgia

The use of radiation in the treatment of the various blood dyscrasias is based on the fundamental principal that an immature cell is more susceptible to its action than one that is mature, therefore, just as in malignancies, it represents an attempt to apply it in such a manner that abnormal cells are destroyed and other tissues affected as little as possible, and in many diseases such palliation as is observed is due in large part to its judicious use. As in other diseases where cell destruction is attempted, roentgen irradiation is used in an attempt to destroy, and therefore remove the excessive number of blood cells, not only in the peripheral blood, but also in their sites of deposition, and in areas of excessive leukopoiesis.[2 3 4 5 6 7 9]

In the leukemias radiation acts almost as a specific in its effect on the various lymphatic nodes, spleen and white cells. It should be emphasized, however, that this method of treatment is exceptionally dangerous in unskilled hands.

One must realize, however, that this treatment does not cure, but rather is an excellent palliative agent, in that the reduction in size of large glandular tumors, or an enlarged spleen, will improve the general physical condition of the patient to such an extent that he can leave the sick room and return to his occupation for variable periods of time. However, it should be anticipated that the time will inevitably come when further treatment will be necessary, and as time goes by these periods of good health become shorter, until finally a stage is reached when there is practically no response to radiation. The chief object of efficient treatment is to delay that time for as long as possible. In general it may be said that the radiologist must be more than a mere technician who administers x-ray treatments on prescription. The cautious administration of x-rays must be the rule always, the doses being extremely small and the patient's response to each dose carefully studied by means of blood examinations, and it should be determined whether or not the destruction of cells is producing dangerous reactions.

This is particularly true when dealing with the type of case showing an enlarged spleen and an exceptionally high white cell count, as too rapid disintegration of the white cells, or reduction in spleen size, may result in unexpected and sudden death of the patient, due to the release of a large amount of toxic material in the circulating blood, these substances being eliminated slowly. It is, therefore, necessary that x-ray dosage be carefully evaluated and kept at a minimum, and, as daily studies of the blood are made, the treatment should not be repeated until the full effect of the previous one has been utilized.

For example, a patient whose white cell count is high on the first day of radiation may show on the following day a slight rise or fall of the leukocytes, which may continue on successive days. Further radiation should not be administered until the count remains stationary for at least two days. By the end of the first 2 weeks a patient's response to radiation will be obtained, and further treatments may be increased, or decreased, in amount according to the reaction.

After there has been a gradual diminution in the size of the spleen, lymph nodes and white cell count, treatments should be discontinued long before the normal is reached, as there will be a persisting prolonged effect of radiation upon these tissues. Therefore, the object of treatment is not to obtain a normal sized spleen or a normal level of the white cells, and if treatment is excessive there may result a dangerous leukopenia. Occasionally it is surprising to find on examination of the blood a white cell count as low as 1,000 to 2,000 cells several months after a course of radiation has been completed, and, therefore, it is important that the treatment not be overdone in the enthusiasm of the radiologist or clinician who usually sees a prompt response and improvement from x-ray treatment.

Acute leukemia is an unusually malignant type of disease, the patient presenting enlarged lymphatic nodes, enlargement of the spleen and perhaps the liver, a tremendous increase in blast cells, with death imminent. It is a debatable question whether the use of x-radiation is of much value. However, as all other methods of treatment are of no value, it seems advisable to administer small doses of radiation, especially to the mediastinum and neck, if there is respiratory distress, and perhaps also to decrease the number of circulating white cells. In my experience this has not resulted in more than temporary relief, as all of these patients die after a short time, usually only a few weeks.

In chronic lymphatic leukemia better results

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from x-ray treatment are seen. This is generally true regardless of whether the patient presents clinical chronicity or hematological chronicity, since the two are usually synonymous. Rosenthal[8] says that roentgen treatment does not prolong life. This is debatable; it certainly does improve the well-being of the patients during their remaining few years.

The action of roentgen ray in both chronic lymphatic and myeloid leukemias is based on its destructive action. It is well to bear in mind that the patient becomes progressively more and more resistant to the action of radiation and finally comes to a time when the lymph nodes or the spleen will no longer recede in size. When this occurs it means that the patient is approaching the end.

The method of treatment employed in the average case of chronic lymphatic leukemia may be presented best by outlining in detail the treatment of a typical case. The following case record will illustrate this:

A 42-year-old white woman complained of enlarged nodes on each side of her neck. She had been in good health until a month before, when she had a sore throat and developed hoarseness. Examination showed a poorly nourished, underweight woman in whom the only positive physical finding was a generalized lymphadenopathy. In the cervical, inguinal and axillary regions there were chains of enlarged lymph nodes. The nodes were matted together, but freely movable, not tender or painful, and not attached to the skin. Also many enlarged nodes could be palpated through the thin abdominal wall. The spleen and liver were normal in size.

Examination of the blood showed 4,100,000 red cells per cu. mm. with 80 per cent hemoglobin and 50,500 white cells per cu. mm., of which 95 per cent were small adult lymphocytes. Biopsy of a cervical node was typical of leukemia (Kracke).[1]

Radiation was directed to all node areas at intervals of five days over a period of three months. The dose never exceeded 110 r to each area and never were more than two areas treated at one visit. This resulted in decrease of white cell count from a maximum of 50,500 to 10,000 and a recession of all lymph nodes so that they were barely palpable, each area receiving a total of 330 r.

Six months later the total white cell count was 7,000 with 50 per cent lymphocytes. During the next nine months the leukocyte count gradually rose to a level of 25,000 with 91 per cent small lymphocytes, with slight enlargement of the lymphoid structures. Radiation was again directed to the enlarged nodes and in thirty days the leukocyte count was normal and the enlarged nodes had disappeared.

At this time, two years later, this patient remains in good health, continues at her occupation, is free from symptoms and presents a barely perceptible lymphadenopathy. Her blood picture is maintained at about the normal level of white cells with the exception that she shows from 75 to 80 per cent small lymphocytes.

Although the above case is presented as illustrative of a suitable method in treating an early case of chronic lymphatic leukemia, it should be again emphasized that the treatment varies and every patient is a law unto himself as to therapeutic requirements. The important principle to be borne in mind is the determination of the maximum dose of effective radiation that will be compatible with the well being of the patient.

Since most patients with chronic myelogenous leukemia have an enlarged spleen and an elevated leukocyte count, the following case is presented to illustrate the method of treatment employed:

A white woman, aged 50 years, had as her chief complaint pain in the left abdomen. She had noticed a mass which had gradually increased in size during the preceding year. She suffered with nausea and vomiting and had lost 20 pounds in the previous two months. Her blood picture, on admission, was: red cell count, 1,450,000; white cell count, 658,000 with the blood picture that of chronic myelogenous leukemia.

She was given a treatment of 200 r direct to the spleen and five days later a second treatment, at which time the leukocyte count had dropped to 400,000. Daily blood counts showed a gradual decrease in the white cell count, so a third treatment was given at the end of five days more. On the second day after the third treatment she had a severe reaction, including a fever of 104 degrees with a chill, and for six days afterwards fever and chills. After this subsided, ten days later, she was given the fourth treatment with the white cell count at 230,000. At this time only 100 roentgen units were administered, whereas the preceding treatments were 200 roentgen units each. Five days later she received another treatment at which time her leukocyte count was 170,000; five days later the sixth treatment with the leukocytes at 85,000. In the meantime, her red cell count had increased to 2,500,000. She was then discharged from the hospital.

She was kept under observation and three months later the red cells were 4,800,000, hemoglobin 80 per cent, and white cells 15,000. Her spleen had receded to where it was no longer palpable. For eighteen months she was in good health and received no radiation.

Two years later her white cell count was 80,000 and her spleen slightly enlarged. The patient then received 1,100 roentgen units given at ten-day intervals with 110 units at each dose. The leukocyte count dropped to 40,000 and the spleen again receded.

After an interval of fourteen months the spleen enlarged and the leukocyte count rose to 84,000. She received 1,100 roentgen units in doses of 220 roentgens at five-day intervals. It will be noted that she received more radiation at each dose in the last series of treatments. Seven months later she returned because of the enlarged spleen with a leukocyte count of 160,000. Note that the interval between treatments becomes shorter and the dose of radiation larger. She received 1,500 roentgen units in divided doses, reducing the leukocyte count to 40,000, but the spleen decreased in size less rapidly than before.

Eight months later the leukocyte count was 156,000. A single dose of 200 roentgen units was delivered to the enlarged spleen with recession of the leukocyte count to

35,000. Fourteen months later the leukocyte count was again elevated to 200,000 and in the meantime the patient had become progressively anemic. This time she received five treatments, a total of 500 r.

It will be noted here that in the six years of treatment this patient received radiation at intervals varying from seven to twenty-four months. All radiation was directed to the spleen and in each instance a prompt improvement took place, including both recession of spleen and regression of the leukocyte count. At no time was radiation applied to the long bones or thorax, and no effort was made to bring the leukocyte count below 30,000 cells per cu. mm.

After seven years this patient was living, but because of increasing anemia with more frequent periods of febrile attacks, radiation had to be used with considerable caution to avoid reactions. Furthermore, the patient had never been confined to her bed except for a few days and during these years has led an active, energetic life. The patient died seven years and three months after the disease was recognized.

Such a case illustrates the judicious and cautious use of radiation therapy. Occasionally a patient is seen in whom the diagnosis of chronic myelogenous leukemia can be established on a basis of marked splenomegaly, and in whom the leukocyte count is at about a normal level. The following case will illustrate:

A white man, aged 50 years, complained of a slightly tender mass in the left upper abdomen and of loss of strength during the preceding few months.

A blood study showed his red cells to number 3,300,000 per cu. mm. and hemoglobin 65 per cent. The leukocyte count was 7,500 with 62 per cent granulocytes and 38 per cent lymphocytes. A study of the granulocytes presented a sufficient degree of immaturity to establish the diagnosis of chronic myelogenous leukemia in the subleukemic phase (Kracke).[1] His blood platelets were also at a low level.

His spleen was given 1,200 roentgen units divided into ten doses during a period of four weeks. On completion of these treatments the spleen had receded apparently to normal size and the leukocyte count had decreased slightly. Three months later his red cell count was 4,600,000 with 92 per cent hemoglobin and the leukocyte count 4,200. Twelve months passed without treatment before he returned because of splenic enlargement. The red cells were normal, the leukocytes numbered 4,200 per cu. mm. Therefore, at this time, this patient was considered to be in an aleukemic state (Kracke).[1] Radiation was directed cautiously to the spleen, a total of 100 roentgen units being given at three-day intervals for five doses. The white cells maintained their level and the spleen receded rapidly in size with marked improvement in the sense of well being in the patient. Eight months later the leukocyte count still was low, being 4,700 per cu. mm., and the red cells were practically normal. The spleen was uncomfortable, but only moderately enlarged. He was then given 600 roentgen units at three-day intervals in 100 unit doses. Six months later he was given 400 more roentgen units directed to the spleen, which was slightly enlarged.

Summary of this case illustrates the method of treating chronic myelogenous leukemia with splenomegaly, but in the aleukemic phase. This patient has been treated for three years as outlined above and is active, in good health, and sheriff of his county.

Another case is cited to illustrate the treatment employed in which splenomegaly and leukopenia were even more marked:

A white woman, aged 48 years, weighing 98 pounds, complained of a tumor which filled the left abdomen, which she had noted slowly growing for twelve months.

A blood study showed the red cells to be 4,100,000 with hemoglobin 50 per cent, and, therefore, a moderately severe hypochromic anemia. The white cells were only 5,000 per cu. mm., and 30 per cent of these appeared to be myeloblasts. The diagnosis (Kracke)[1] was acute aleukemic myelogenous leukemia.

In spite of the decreased leukocyte count, this patient was given 100 roentgen units at two-day intervals through a small cone 6 x 6 cm. distributed over multiple ports to the enlarged spleen for a total of 600 r. Two weeks later the leukocyte count was 1,600 with 20 per cent blast cells, the platelets were low, and radiation therapy was discontinued. Monthly reports from her physician stated that the spleen had returned to the level of the costal margin, that she was enjoying good health, that the white cells averaged about 3,500 per cu. mm. and she had gained forty pounds. Eight months later the spleen had enlarged to three times its normal size and the leukocytes had reached a level of 5,500. At that time a dose of 300 roentgen units of radiation were directed to the spleen at intervals of four days to the total of 1,200 r. The white cells fell to 2,700 and the red cell count remained unaffected. Following this the spleen receded and six months later she received two treatments of 100 roentgen units each, which was followed by a severe reaction with chills and fever. Three months later she was given an additional series, which was followed by a severe reaction after a total of 300 roentgen units had been given. Two years after the initial treatments the white cell count was 4,100 with the spleen moderately enlarged, but otherwise her general health was fair, and she was leading a fairly active, normal life. She died two years and eight months from the time the disease was recognized.

The treatment of this patient illustrates the radiation that can be employed in a patient with a large spleen in the aleukemic phase, who apparently borders on the development of acute myeloblastic leukemia.

In a discussion of the x-ray treatment of hemorrhagic purpura (idiopathic thrombocytopenia) several problems arise: (1) whether or not radiation may be regarded as a cure for this disease, or if it is merely an aid in improving the general condition of the patient to permit splenectomy with as little danger as possible; (2) how well does the spleen respond to treatment;

and (3) does radiation produce fibrotic changes that would make subsequent splenectomy more hazardous. It is my opinion that the spleen is receptive to radiation and that thorough radiation of the spleen will produce practically the same end result that is accomplished by surgical removal. Many writers have reported complete atrophy of the spleen following radiation and if the spleen is reduced to a non-functioning gland the same result is obtained as that accomplished by surgery. The following two cases are illustrative:

A girl 13 years old presented all clinical signs of purpura hemorrhagica. There were hemorrhages from the gums and mucous membranes of the mouth and over the conjunctival surfaces of the eyes, with large purpuric spots over the buttocks, cheeks and hands. The spleen was not palpable and the cervical nodes were enlarged. Blood count was 3,380,000 red cells; 19,420 white cells and 53 per cent hemoglobin. The differential white count was neutrophils 84 per cent, lymphocytes 15 per cent, eosinophils 1 per cent, platelets 220,000, coagulation time 3 minutes, bleeding time 31 minutes. Blood was found in the urine. A transfusion of 500 c. c. of whole blood was given and two days later 200 c. c. were given. The hemorrhagic areas appeared worse, new lesions appeared about the eyes and over the face and body. The amount of blood in the urine increased. At this time the platelet count was 90,000 and two days later it was 20,000. Evidently the disease was increasing in severity. On the fourth day of her illness radiation was directed to the spleen through a lateral port. Two days later a second treatment was applied through the anterior surface. Each treatment was 600 r at 200 kilovolts, 10 ma. to 0.75 mm. copper and 1 mm. aluminum filter, 50 cm. skin target distance. After the first treatment she showed unmistakable signs of improvement, which continued daily, and she was discharged from the hospital nine days after admission, all blood having disappeared from the urine with fading of the hemorrhagic areas. X-ray treatment was continued until a total of 3,000 r were delivered into the spleen through three ports. This girl has remained completely well during the past seven years.

Case 2.—A white woman 35 years old had many large purpuric spots over the entire body and hemorrhages from all the mucous membranes, which had shown most activity at the time of menstruation. During the previous six months her menses had been unusually profuse, requiring confinement to bed for the previous two months. She had also severe nasal hemorrhages, bloody stools and blood in the urine. The blood count was: 3,800,000 red cells; white cells, 5,770; hemoglobin, 70 per cent; blood platelets, 9,000 per cu. mm. X-ray treatment was instituted with two objects in view: first, destruction of the spleen, and second the production of an artificial menopause. These treatments were completed in nine days. After the second day no more new hemorrhagic areas appeared under the skin or in the mucous membranes. She was discharged from the hospital on the tenth day with no recurrence of purpuric manifestations. However, she should undoubtedly have further radiation in order to produce a complete fibrosis of the splenic pulp, to prevent the occasional purpuric spot which she now shows. Unfortunately she lives a long distance in the country and inasmuch as her general health is satisfactory, she has neglected to obtain further radiation. A letter five years later reported her health as excellent.

Polycythemia vera is another blood dyscrasia occasionally encountered with a red cell count often above 7,000,000 per cu. mm. Treatment of this disease has included drugs such as phenylhydrazine to depress the bone marrow, and to prevent the formation of red cells. The response to this drug is often severe, it being a very dangerous method of medication. There are many reports in the literature concerning the use of radiation to the bone marrow as a means of preventing the formation of red cells. This is based on the known fact that in the treatment of malignancies patients who have been subjected to radiation over long periods of time always develop a severe anemia. A satisfactory method of treatment by radiation is to select only two bones, such as the femurs, and to give sufficient radiation to cause a fall in the red cell count. The amount of treatment required is very little as measured in roentgen units. Treatments should be discontinued when the blood count is below a normal level. It may be repeated several months later when the red cell count again reaches a high level, then stopping treatment when a slightly subnormal level is reached.

The time ultimately arrives when further treatment of the femurs will not produce a reduction in cells due to bone marrow damage. Then an additional bone such as the humerous should be treated. Following this technic x-ray treatment may be continued for many years, maintaining the patient in a state of well being and comfort and permitting him to pursue his occupation. The following case is illustrative of this method of treatment:

A student, 20 years old, was found to have a red cell count of 8,500,000. He was treated with phenylhydrazine followed by a very severe reaction which almost cost him his life. It did, however, decrease his blood cells to within normal limits. One month later the red cell count was again approximately 8,000,000 per cu. mm., and he refused further drugs. Radiation was directed to the femurs on alternate days until each femur had received 1,000 r. Treatment was then discontinued, as the count was 5,300,000, and one month later it was just over 4,000,000. In six months his count had returned to 7,500,000 and 600 r additional were given to each femur in doses of 300 r at three-day intervals. A prompt fall in the red cells to below 5,000,000 occurred. He has not required any further radiation in the past sixteen months and has attended college.

SUMMARY

If possible, the amount of radiation given to a patient, not only directed to the spleen, but to any part of the body, should be within the

limits of tolerance so that no reactions will occur. This is especially important in patients who are ill and debilitated. Since reactions are most likely to occur following radiation of the upper abdomen, including, of course, the spleen, dosage should be carefully regulated when it is applied to that area. It is important, of course, to prevent reactions in every way possible. If the treatment is given when the patient has an empty stomach, reactions are less likely to occur. It is thought that preliminary evacuation of the bowels is helpful. The limit of dosage should be such that the products of broken down tissue will not give rise to a toxic reaction in the days following.

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DISCUSSION (*Abstract*)

Dr. Robert J. Reeves, Durham, N. C.—Little more can be added to Dr. Clark's discussion of this subject except comparison of different methods of therapy. In considering the question of why some patients respond to x-ray better than others with essentially the same blood picture, we should keep in mind that every case of leukemia is different and the routine of roentgen therapy varies with each individual case. We believe a close check on the platelet count is most important. If the platelet count continues low, a bad prognosis can be predicted.

The method of "spray therapy," or long distance irradiation, is gaining a wider recognition. Hunter, in 1936, presented a paper, using this method in the treatment of leukemia and polycythemia. Pancost advised using this method over the long bones as early as 1906. The method apparently fell into bad repute because the dosage was too large.

Golden and McAlpin, in 1931, presented a very thorough study, advocating the small fractional dose method and stressed the importance of the close cooperation of the hematologist and internist.

All patients with lymphatic and myelogenous leukemia coming into Duke Hospital are treated by the spray technic with supplementary small doses to the spleen. This can usually be kept up for the first two or three years. In order to prove that this method gives longer remissions, two patients may be studied whose blood picture is similar. One case is given three treatments of 100 roentgen units at one meter distance, and blood counts are taken up to twenty-one days. The remission will be from six to nine months. The second case is given 200 roentgen units at a short distance, one to ten-day intervals, for twenty-one days. The drop in blood count will be greater. The remission will be very short. Our technic is 200 kilovolts one meter distance, 0.5 mm. copper filter: a dosage of 50 roentgen units, alternating front and back of the body, giving not more than 300 units. If supplementary therapy to the spleen is given, a dosage of 200 units at a short distance is given.

The complication of pregnancy in cases with leukemia brings up the question whether there should be an early interruption. Kaplan, in 1932, reported a case of a 26-year-old multipara presenting symptoms of myeloid leukemia fifteen months before admission. The blood picture was controlled by irradiation and a normal child was delivered. There were no untoward results three years later.

Hofstein, in 1931, found twenty-eight cases in the literature, thirteen of which were acute. Eleven were chronic and bore living children. Four aborted. In the advanced stage of the disease the condition is aggravated by pregnancy. This last statement, however, has not been verified in one of our cases of chronic myeloid leukemia.

A woman of 30 years, seen April 4, 1934, with weight loss, an enlarged spleen, leukocytosis of 46,000 and a large number of myelocytes in the blood smear, received 200 r of x ray at infrequent intervals and responded very well. Three years later, on July 14, 1937, the white count was 37,500 and a dosage of 100 r at 100 cm. distance was given. On September 17, the count was 27,000. At that time she had missed a menstrual period. She is now four months pregnant and the blood picture is essentially normal.

For a number of years thorium dioxide has been used in the hope that either the low-grade radioactivity of the thorium or its activation after being exposed to high voltage therapy might be beneficial, but results have been disappointing. Dr. Coe, of Washington, has treated three cases. One of these was diagnosed in 1927 as myeloid leukemia and in 1929 thorium was given and no x-ray has been given since. The patient has remained well, but he does not feel that the thorium had anything to do with the remission.

In agranulocytosis, there is varying opinion as to whether x-ray therapy is of value. We have found that small stimulating doses, 10 to 20 per cent of an erythema dose, will in some cases be of definite benefit. The action is indirect through the formation of substances in the skin or blood which induce an outpouring by the bone marrow of large newly formed, rapidly maturing white cells. Three treatments are given on successive days. Waters and Firor treated four cases and all recovered. All received transfusions, but none responded before x-ray was given.

In polycythemia vera, roentgen therapy is very helpful. Hunter has written a very complete treatise on this subject. He advocates the spray technic, using 25 to 50 r with a total dose of 200 to 300 r. A dosage of 25 r may be given daily for six days, allowing a rest period of one week and repeating six more treatments. This usually

produces marked improvement and can be kept up at intervals for many years.

In summing up the various methods of treatment of the blood dyscrasias, we advocate the spray or teleroentgen therapy supplemented by local regional therapy. This method, when administered properly and watched closely, has given very satisfactory results.

A FATALITY FROM ACUTE HEMOLYTIC ANEMIA WHICH DEVELOPED DURING THE ADMINISTRATION OF SULFANILAMIDE*

By HAROLD WOOD, M.D.
Charleston, South Carolina

On the autopsy service of this department the opportunity recently occurred to make a postmortem examination on the body of a Negro whose death was attributed to acute anemia incident to the therapeutic use of sulfanilamide. This case is reported for the purpose of corroborating the implication in Harvey and Janeway's† paper that sulfanilamide may produce sufficient hemolysis to cause death from anemia, and to re-emphasize the necessity of immediate transfusion when such an anemia is manifested. There was no evidence in this case to indicate whether the individual was or was not abnormally susceptible to toxic effects of this drug.

The following clinical and laboratory data were submitted to me for use in this report:

The patient was a 28-year-old Negro whose illness began with a prolonged chill followed by sharp pain in the right side of the chest, exaggerated on breathing and coughing. The following morning, November 30, 1937, he began coughing up reddish brown sputum and was first seen by a physician on that day. Examination revealed him to be well developed and well nourished, with hot, moist skin, and coated tongue. He appeared acutely ill. His temperature, by mouth, was 101° Fahrenheit, the pulse rate was 92, the respiratory rate was 26, and the blood pressure 120/90. Over the right lung areas there were increased tactile fremitus and voice sounds, with tubular breathing and dullness to percussion, and in the posterior superior area fine rales were heard. Percussion over the right axilla produced pain. The point of maximum intensity of the cardiac impulse was at the sixth intercostal space, 10 cm. to the left of the midsternal line, and the rate was accelerated, but no other abnormalities were elicited. There were no other significant physical findings. A provisional diagnosis of lobar pneumonia was made.

The second day of observation, December 1, pneumococcus Group IV was reported from a sputum specimen. The following day pneumococcus Group IV was reported from a blood culture. This organism was later said to be an hemolytic streptococcus. On the sixth day of observation, December 5, an hemolytic streptococcus was reported from a second blood culture. The disease was then considered to be a streptococcal pneumonia, with septicemia.

Sulfanilamide therapy had been begun on the third day on the basis of a grain of the drug for every pound of body weight per day administered by mouth, the first dose 40 grains, then at the rate of 30 grains every four hours. This dose was reduced to 20 grains every four hours on the sixth day.

The general condition of the patient improved, and by the seventh day there was evidence of resolving pneumonia at the base of the right lung. However, two days previously jaundice had been observed, and there had been a severe reduction in the hemoglobin and the erythrocyte count (see chart). Jaundice was noticed until the twelfth day and there was a further reduction in hemoglobin and in the erythrocyte count. The leukocyte count first had increased during sulfanilamide administration and then had decreased markedly. With the increasing anemia the erythrocytes exhibited anisocytosis and poikilocytosis, and the patient complained of persisting headache. After some difficulty a blood donor was secured, and on the twelfth day 300 c. c. of citrated blood with 150 c. c. of saline was given, with slight improvement in the patient's condition. Another donor was secured with difficulty and four days after the first transfusion a second transfusion of 500 c. c. of citrated blood was given. In the interval between transfusions the patient had vomited on three occasions, had bled from the gums, was hardly able to swallow the day before the second transfusion, and had become irrational and slightly hyperactive. He died approximately six hours after the second transfusion. There was no sign of unfavorable reaction to either transfusion. Death occurred 16 days after the illness began.

The accompanying chart shows the temporal relation by days of some of the clinical observations, therapeutic procedures, and laboratory determinations. In addition the blood Wassermann and Kline tests were each strongly positive, and on one instance the urine contained a few hyaline and granular casts.

The medications administered besides the sulfanilamide during the period of observation were: morphine sulfate, four 1/6 grain doses; codeine sulfate, eleven ½ grain doses; sodium bicarbonate, 1 oz.; sodium bromide, 30 grains; cascara sagrada, 2 oz.; milk of magnesia, 1 oz.

ABSTRACT OF AUTOPSY PROTOCOL*

The postmortem examination was made four hours after death. The subject was well developed, well nourished, and of average stature. There was no apparent jaundice of the sclerae, and on section there was no evidence of jaundice of the soft tissues or the serous surfaces. The serous cavities contained no excess of fluid. There were a few pleural adhesions involving the lower lobe of the right lung posteriorly.

*Received for publication April 9, 1938.

*From the Department of Pathology, the Medical College of the State of South Carolina, Charleston.

†Harvey, A. M.; and Janeway, C. A.: The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide. J.A.M.A., **109**:12-16 (July 3) 1937.

*Autopsy No. 37-224.

The heart weighed 400 grams (not considered excessive for the size of the individual) and exhibited no anatomical abnormalities. There was slight intimal and adventitial thickening of the aorta.

The lung surfaces were smooth, except for the pleural adhesions mentioned above. The tissue of all lobes was crepitant, but the right lower lobe was slightly indurated, although there was no definite consolidation. The bronchi and pulmonary arteries were patent.

The liver weighed 1,800 grams. The costal margin was sharp, but the capsule was smooth. The lobular markings of the cut surfaces were fairly distinct, and there appeared to be slight bile staining of the tissue, but this was not intensified after immersion in formaldehyde for a few minutes. The gallbladder was of average size and contained green viscid bile.

The spleen was slightly enlarged and weighed 200 grams, the capsule was quite tense, and the pulp was soft, with prominence of follicles.

Each kidney weighed 300 grams and the capsules were

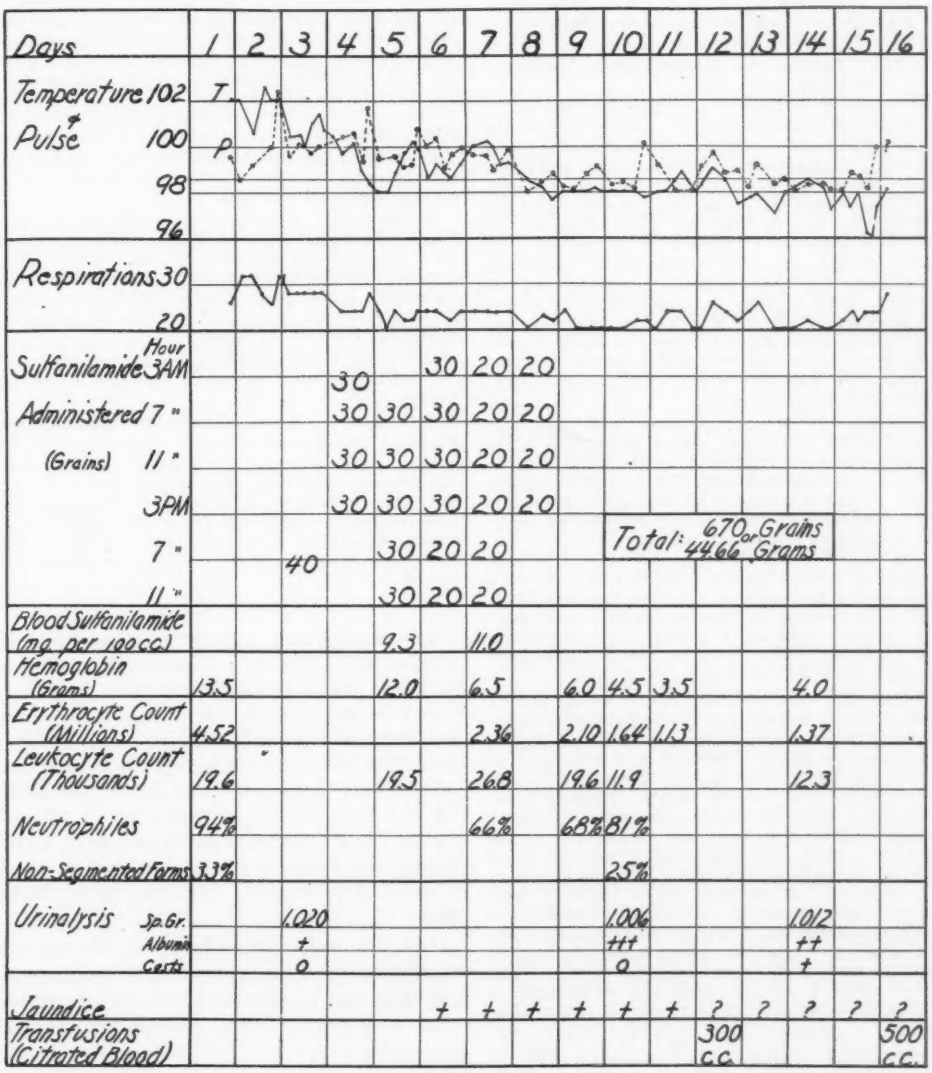
Days 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Temperature 102
Pulse 100
98
96
Respirations 30
20
Hour
Sulfanilamide 3AM 30 30 20 20
Administered 7 " 30 30 30 20 20
(Grains) 11 " 30 30 30 20 20
3PM 30 30 30 20 20
7 " 40 30 20 20
11 " 30 20 20
Total: 670 or Grains 44.66 Grams
Blood Sulfanilamide (mg. per 100 cc.) 9.3 11.0
Hemoglobin (Grams) 13.5 12.0 6.5 6.0 4.5 3.5 4.0
Erythrocyte Count (Millions) 4.52 2.36 2.10 1.64 1.13 1.37
Leukocyte Count (Thousands) 19.6 19.5 26.8 19.6 11.9 12.3
Neutrophiles 94% 66% 68% 81%
Non-Segmented Forms 3.3% 25%
Urinalysis Sp. Gr. 1.020 1.006 1.012
Albumin + +++ ++
Casts 0 0 +
Jaundice + + + + + + ? ? ? ? ?
Transfusions (Citrated Blood) 300 cc. 500 cc.

Chart 1

The temporal relation of certain clinical observations, therapeutic measures, and laboratory determinations.

slightly adherent. The parenchyma was darker in color than usual, and was stippled red here and there. Both the cortex and the medulla of each kidney was widened. The pelves and the ureters were not dilated and the bladder was moderately distended with clear yellow urine.

Section of the brain revealed minute red foci in the white matter, and the fluid of the lateral ventricles was slightly cloudy.

Bone marrow from the sternum and the lumbar vertebra was moist and dark red. Marrow from the proximal and distal ends of the shaft of the right femur and from the proximal portion of the shaft of the right tibia was yellow and greasy.

The gastro-intestinal tract, the pancreas and the adrenal glands showed no lesions.

Histological Examination.—The lungs showed areas of atelectasis with hemorrhage and edema, and in the alveoli of those areas there were a few leukocytes and many large mononuclear cells with brown and black pigment granules in the cytoplasm. Much of this pigment stained blue with the Prussian blue method for the demonstration of iron pigment. There was no evidence of fresh pneumonic exudate in the sections.

Liver sections stained with hematoxylin and eosin showed granular yellow pigment in the cells of the supporting tissue between the liver cell cords. Sections subjected to the Prussian blue reaction revealed blue stained pigment granules in the cytoplasm of practically all of the reticulo-endothelial cells, and in the majority of the liver cells there were blue granules scattered through the cytoplasm.

The splenic sinuses were prominent and filled with erythrocytes, and there was relative prominence of the supporting tissue as compared to the pulp. In the hematoxylin and eosin-stained sections yellow pigment granules were seen in some of the cells of the supporting tissue. The Prussian blue reaction revealed an abundance of granular, blue stained pigment within the cytoplasm of elongated and branching cells situated between the sinusoids, presumably the reticular cells. Little if any pigment was present in the elongated cells lining the sinusoids, and the Malpighian corpuscles were practically free of pigment. Practically no extra-cellular pigment was present in the tissue, and the capsule and trabeculae contained no pigment.

The convoluted and collecting tubules of the kidneys contained casts of globular and granular yellowish-brown pigment, which resembled hemoglobin casts, as well as small amounts of cellular debris. In sections exposed to the Prussian blue reaction a small proportion of that pigment stained blue, but the most of it remained unstained. The cytoplasm of the epithelial cells of the collecting tubules, and to a less extent that of the convoluted tubules, contained granular pigment which reacted positively to the iron stain. The capsular spaces of the glomeruli and the renal calyces contained small amounts of pigment similar to that in the tubules. In the stroma, especially at the junction of cortex and pelvis, there was relatively active leukocytic infiltration. The sections of kidney resembled those of cases of black water fever, but there was no evidence of malaria pigment or parasites in sections of spleen, liver, or brain.

Bone marrow sections from the sternum and the lumbar vertebrae showed hyperplastic hemopoietic tissue. In sections of marrow from the proximal portion of the right femur there were a few small foci of hemopoietic tissue scattered among fat cells, and in sections from the distal end of the right femur and the proximal end of the right tibia the marrow was entirely fatty, with no foci of hemopoietic tissue.

The differential myeloid cell* count, based upon the average of the percentages from four counts of 200 cells each, observed in approximately 40 small fields of a section of undecalcified marrow from the lumbar vertebrae stained by Giemsa's method, was as follows: Basophil erythroblasts, 1.7 per cent; polychromatophil erythroblasts, 37.8 per cent; normoblasts, 7.3 per cent; erythrocytes, 13.1 per cent; heterophil promyelocytes, 0.7 per cent; heterophil myelocytes, 11.1 per cent; heterophil metamyelocytes, 7.8 per cent; heterophil leukocytes, 4.0 per cent; eosinophil promyelocytes, 0.1 per cent; eosinophil myelocytes, 1.0 per cent; eosinophil metamyelocytes, 1.8 per cent; eosinophil leukocytes, 1.1 per cent; megakaryocytes, 1.3 per cent; unidentified cells, 12.6 per cent.

In the pons and in the white matter of the cerebrum there were a few minute foci of hemorrhage, but no other lesions were discerned.

The adventitia of the aorta was thickened and vascularized, the media was vascularized, and in both coats there was perivascular round cell infiltration. There was slight hyaline and fibrous thickening of the intima. Para-aortic lymph nodes attached to the adventitia of the section showed prominent hyperplasia of the reticulo-endothelial tissue of the sinuses.

Low grade chronic inflammatory fribrosis and round cell infiltration were present in the wall of the gall-bladder.

Sections of the heart, pancreas and adrenal glands showed no lesions.

The autopsy diagnosis was hemolytic anemia. There was hemosiderosis of the liver, spleen and kidneys, with hemoglobin casts in the kidneys. There were pulmonary hemorrhages, petechial hemorrhages of the brain, and hyperplasia of the erythropoietic element of the vertebral and sternal marrow, syphilitic aortitis and chronic cholecystitis.

CONCLUSIONS

(1) During the administration of sulfanilamide an acute hemolytic anemia may develop, of sufficient degree to produce death.

(2) In this case the hemolytic streptococcal infection may possibly have been a factor in producing hemolysis; however, the clinical indications were that the infection had subsided during the sulfanilamide therapy.

(3) The development of an hemolytic anemia during sulfanilamide therapy is indication for prompt, and probably repeated blood transfusion.

(4) The pathological findings in this case were representative of any severe hemolytic anemia, and there was no feature which could be considered as a specific lesion produced by the sulfanilamide.

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*The terminology used here follows that of Maximow and Bloom in their Textbook of Histology, Second Edition, pp. 80-88, 1935.

THE CUMULATIVE EFFECTS OF PENTOTHAL SODIUM*

By J. Ross Veal, B.S., M.D., F.A.C.S.
and
Chapman Reynolds, B.S., M.D., F.I.C.A.
New Orleans, Louisiana

Our clinical experience with sodium evipal and pentothal sodium has convinced us that these drugs have a definite place among modern anesthetic agents.[1] On the other hand, although we have employed them only in minimum doses and for such brief procedures as the incision and drainage of abscesses and the removal of packs, we have been impressed with the wide variation in individual susceptibility to them. One patient may recover from the narcosis within five minutes. Another, given the same dose, may not recover for twenty or thirty minutes. Still another may react briefly and then relapse into a prolonged sleep. These pronounced variations produced by single doses interested us in the possible effect of repeated doses, and we undertook three sets of experiments to determine this point.

Pentothal sodium (sodium-ethyl, l-methyl butyl thiobarbituric acid) in 5 per cent aqueous solutions was used in all the experiments, which were performed on both dogs and cats. This drug differs from pentobarbital sodium (nembutal) in that one atom of oxygen has been replaced by an atom of sulphur on the urea side of the molecule.

When dogs were used the carotid artery, jugular veins and trachea were exposed under local (procaine hydrochloride) analgesia. When cats were used, a preliminary light ether anesthesia was administered before these structures were exposed. The carotid artery and trachea were each cannulized and connected to a recording drum, and the injections of the drug were made into the jugular veins.

(1) In the first group of experiments we employed fractional dosages and used both dogs and cats. An initial dose of 20 mg. per kg. of body weight was administered slowly, during which time the carotid blood pressure and the respiratory rate were recorded simultaneously on a kymograph drum. The animal was then observed and tested at intervals to establish the return of the reflexes. As soon as they had returned, small fractional doses of from 3 to 5 mg. per kilo of body weight were administered with small amounts of saline solution through a cannula in the femoral vein. After each dose the duration of anesthesia and the time at which the reflexes had returned were recorded. At the end of each recovery period additional doses were administered in the same manner.

Generally speaking, with each additional dose there was a gradual lengthening of the duration of the anesthetic action of the drug. After the initial dose the period of anesthesia ranged from 7 to 20 minutes. As the fractional doses were administered, the duration of anesthesia increased, lasting from 40 to 50 minutes. Finally, without any indication from the blood pressure or respiratory rate, both of which were under continuous observation, an additional fractional dose would produce death.

The animals varied widely in their tolerance to the drug. One animal tolerated a total fractional dose of 125 mg. per kilo administered over 11 hours, but the final dose precipitated death, although the reflexes were not abolished. Another animal remained anesthetized for 45 minutes after the initial dose of 20 mg. per kilo, and 3 additional fractional doses of 3 mg. per kilo given at 15-minute intervals did not abolish the reflexes or cause a cessation of respiration. When the fourth dose, in the same amount, was administered, respiration suddenly ceased, the blood pressure fell to zero, and all efforts at resuscitation failed. In this particular animal the total dose given over a period of 90 minutes was only 32 mg. per kilo; the initial dose was well tolerated, but the cumulative action of the repeated small fractional doses caused death.

(2) In the second set of experiments an initial dose of 20 mg. per kilo of body weight was given slowly by the intravenous route, and produced complete anesthesia, of an average duration of 20 minutes. As soon as the reflexes had returned, the same dose was repeated; it produced a much more profound anesthesia, a cessation of respiration and a marked fall in blood pressure, and some of the animals died. With additional doses in the same amount given as soon as the reflexes returned, the effect was greatly exaggerated over the initial dose, and none of the animals tolerated as much as 100 mg. per kilogram of body weight.

These experiments seem to indicate that the animals could destroy or break down to some less toxic form of barbiturate only a certain amount

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*From the Departments of Surgery and Pharmacology of the School of Medicine of Louisiana State University, New Orleans.

of pentothal sodium over a given period of time. If additional amounts were added, the cumulative action was lethal.

(3) In order to study the effects of pentothal sodium when it is absorbed more slowly than by the intravenous route, we administered the drug to a series of cats by intraperitoneal injection. Each animal received an initial narcotic dose of 25 mg. per kilo of body weight; the duration of the narcosis ranged from 35 to 100 minutes. As soon as the animals began to hold up their heads and try to get to their feet, a second, similar dose was given by the same route; the duration of the narcosis ranged from 63 minutes to 6 hours and 36 minutes. When a third similar dose was given, the duration of narcosis ranged from 3 hours and 7 minutes to 5 days. Forty per cent of the animals died, although they recovered from the narcosis and were able to take nourishment. Death ensued gradually, in coma, and not abruptly, as when the drug was administered intravenously.

In this set of experiments a presumably adequate time was allowed for the destruction of the minimum dose of the drug which had been used, but with each additional dose its action was greatly prolonged. The onset of narcosis after the intraperitoneal injection was prompt, but the subsequent course more closely simulated the effect of nembutal or amytal than of pentothal sodium.

These three sets of experiments show that when pentothal sodium is given in minimum narcotic doses, there is prompt narcosis and equally prompt recovery from it, although the recovery from narcosis and the return of the reflexes does not necessarily indicate that the action of the drug has been completed. Small additional doses produce profound narcosis of longer duration than the initial dose, which would seem to indicate that the drug is not completely destroyed within the time required for recovery from its narcotic action. It would also seem to indicate that the organism is able to destroy or to change to another form of barbiturate only a certain amount of pentothal sodium over a given period of time. Part of the initial dose remains in effect, and there is a cumulative action when additional doses are employed.

Gruhzit[2] and his associates have called attention to the possible histopathologic changes produced by the barbiturates, and their work seems to suggest two possibilities: that normal organs are incapable of destroying more than a certain amount of these agents, and that their effect may be to cause changes in the organs which would make them lose their capacity to break down and destroy such drugs.

The statement has often been made that pentothal sodium is broken down rapidly in the body, and that the injection of small fractional doses is comparable to the administration of ether by the open drop method. Our experiments throw considerable doubt upon that statement. They prove that this drug is not so rapidly destroyed as clinical reports of its use lead us to believe. The rate of recovery from anesthesia and narcosis is rapid when the minimum dose is administered. When additional doses are administered there is a cumulative effect and the duration of narcosis or anesthesia is prolonged. With each additional fractional dose the margin of safety becomes less, and a lethal dose may be administered without any warning from the changes in the respiration, circulation and reflexes.

The conclusion is that until the ultimate disposition of pentothal sodium in the body is determined, it is not a safe agent for prolonged anesthesia, even by the fractional method of administration.

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CIRCULATORY VERSUS RESPIRATORY DEATHS FROM PENTOTHAL SODIUM*

By CHAPMAN REYNOLDS, B.S., M.D., F.I.C.A.
and
J. ROSS VEAL, B.S., M.D., F.A.C.S.
New Orleans, Louisiana

Early observations[1] on the action of pentothal sodium stressed the arrest of respiration while the circulation was still apparently in good condition. Recovery usually took place spontaneously, or with artificial respiration, or following administration of one of the common analeptics with or without artificial respiration. This impression was based mostly on the effects of single doses.

Since with most anesthetics it is usually not

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*From the Departments of Pharmacology and Surgery, School of Medicine, Louisiana State University, New Orleans.

difficult to restore respiration if the circulatory apparatus is relatively intact, this drug would seem to be fairly safe when used with discretion. In laboratory use of dogs and cats we devoted particular attention to the state of the blood pressure in different degrees of anesthesia and its relation to respiration.

METHODS

No preliminary anesthetic was used. With careful procaine local analgesia and gentle manipulation, cannulae were fixed in the trachea, the carotid artery, and the femoral vein. Pain was not evidenced; occasional excitement occurred, only paralleling the previous nervousness and disposition of the animal. Thus the dosage of pentothal sodium used was not distorted by unknown concentrations of residual general anesthetic.

RESULTS

A slowly given single injection of an amount of pentothal sodium just beyond the borderline of tolerance stopped respiration without any measured fall of blood pressure. In many instances there was a rise of a few millimeters. After return of reflexes, a second dose almost always elicited a sudden change in the blood pressure curve, with a slow rate and an increased "pulse pressure." This was noted by Gruber,[2] and his electrocardiographic investigation enabled him to explain it as being due to the development of ectopic ventricular contractions separated by long compensatory pauses. Without further medication, this peculiar slow rhythm disappears as suddenly as it appears. It does not indicate any significant alteration of the systolic pressure.

If suspense of respiration is allowed to continue, there is the usual transitory (asphyxial) rise followed by the usual gradual fall of blood pressure to 0, with the ventricles still feebly contracting for a short time. Here artificial respiration will ordinarily resuscitate, if not too much total pentothal sodium has been given. (We had one instance of 18 consecutive resuscitations during one hour and fifty minutes, with cardiac death finally occurring without immediate warning.) Pictrotoxine, alpha lobeline, coramine and metrazol were tried when artificial respiration seemed not promising, or became too tiresome. There was a fair incidence of apparent benefit, with the impression that metrazol was the most efficient. In a few instances of prolonged anesthesia, the pentothal sodium solution included 1:500,000 epinephrine. No essential benefit was seen.

There comes a time, however, while keeping the animal just at the point of abolition of corneal reflex by repeated small injections of pentothal sodium, that suddenly the blood pressure drops to 0. Analeptics, intracardiac epinephrine, cardiac massage and artificial respiration give only a temporary rise or none at all. The suddenness of the blood pressure fall and the previous appearance of ectopic beats indicate the possibility of ventricular fibrillation.

It is perhaps significant that in cats with two or three repeated minimal anesthetic doses intraperitoneally, respiration continued for as long as two to five days before the unconscious animals finally died.

SUMMARY

Acute moderate overdosage of pentothal sodium is first manifested by cessation of respiration.

With continuous administration of small amounts, only enough to maintain light anesthesia, signs of heart muscle poisoning appear without warning.

No matter how gradually and how carefully given, the longer the administration is continued, the more does the danger seem to shift to the circulatory side, where nothing much can be done about it.

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INDUCTION OF ANESTHESIA*

By ANSEL M. CAINE, M.D.
New Orleans, Louisiana

The object of this paper is to emphasize some well known principles that are often ignored rather than to detail technic. The frequent disregard of these fundamentals is its excuse.

As in everything else in life, a good start is a great help. First impressions are lasting. How guarded should be our words and actions at the commencement of anesthesia, yet how assured! Lack of assurance in the presence of the patient has no place in anesthesia. All a patient knows about the whole procedure is the induction of and recovery from the anesthetic, so every effort

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should be made to render both of these phases of anesthesia as free from discomfort as possible.

There should be a preliminary visit by the anesthetist to the patient whenever possible. This is not always convenient, and is sometimes almost impossible, in the case of patients coming into the hospital a short time before the time set for the operation. For economic reasons, in recent years some patients come into the hospital from 7:00 to 9:00 o'clock the evening before a major operation scheduled for early morning hours. With the history to be taken by the intern, the preliminary night-before-orders to be carried out by the nurse, and so on, the anesthetist is often shut out. Then, with the early schedule next morning, together with premedication, there is little time to become acquainted with these patients. But often these conditions do not exist, the patient being in the hospital quite long enough to be seen ahead of time.

This part of the anesthesia is very important and often neglected by the busy anesthetist. The obstacles in the way and time actually lost in trying to see these patients is most discouraging and conscience-searing.

Let us dig in our cleats, and, in an ever-positive way, try to eliminate these obstacles. Continually stress the early arrival of patients in the hospital and its importance. For those hospitals which have no such rule, try to establish a checking-out hour early enough in the afternoon so that these beds can be made ready for new patients to occupy so that their histories may be taken before late in the night. Hotels have around 6:00 o'clock as the checking-out hour. Two o'clock would be more nearly the right time for hospitals. This would eliminate the economic excuse for the late arrival of patients in the institution for a longer than one-day stay. All rules have exceptions, but those exceptions should be for good reasons.

Knowing the scheduled operation, and reading the history, the anesthetic agent to be used will probably be decided at this visit. If the risk is poor or doubtful, and further information is desired, the surgeon can be reached. Good surgeons do not step in the dark, but work their cases up and are in position usually to give the information desired, which is not obtainable at the visit of the anesthetist.

Some remarks on premedication are *apropos*, as this is an important step in induction of anesthesia. While carried out more or less routinely in general surgery, it is still a much neglected field in throat surgery. The reason given is that these drugs dull the throat reflexes and thus might be a factor in concealing bleeding following operation for tonsillectomy and adenoidectomy.

With careful hemostasis at the operation, the obtunding effect of preliminary medication on the throat reflexes should be about gone before bleeding appears. A patient with an oozing throat should not be returned to his bed. The routine value of premedication far outweighs the remote possibility of its blinding a postoperative hemorrhage. To allow nervous children to come to the surgery without some help along this line, when it is safe, seems wrong to us. A consideration of some of the things we subject these children to, as a routine, might give us pause.

(1) They are allowed no breakfast that they are accustomed to.

(2) They are bundled up and taken to a hospital and into environments that they are not used to.

(3) In an effort to render them less nervous, the parents sometimes deceive them as to the cause of the visit to the hospital.

(4) They are sometimes operated upon late in the day, if there are several cases on the surgeon's list.

(5) They sometimes pass a truck bearing a patient to or from the operating room, with distressed relatives accompanying him.

(6) They are brought to the operating room by a strange person, the parents toddling along trying to reassure them when their own hearts are wrung over the matter.

(7) They are placed on a table in a, to them, terrifying room, where caps, gowns, draperies, masks, and sometimes instruments, predominate. New and horrible odors, never noticed by the attendants, meet their nostrils.

(8) It may be that the crying of a similar victim in an adjoining operating room is heard by the child.

(9) There is an unconscious lack of sympathetic feeling on the part of the surgeon and attendants for the child and the parents. By this time the child is sometimes quite terrified and is clinging to a parent's neck begging for mercy. In order to be heard above his screams there is more or less loud talking by the parents, the nurse and the anesthetist.

(10) Finally, after failure at reasoning under these conditions, the child is held down and the mask applied. If gas is given, the struggle is short, but the feeling of suffocation on the part

of the child is present under these conditions, it matters not what the agent used. If ether alone is used, it is worse and prolonged.

While this is not always the picture, it is frequent enough to be quite familiar. We are unkind enough to say the child is bad. The surgeon might chime in and say that he expected us to have trouble, for he had trouble with him in his office. It is not badness. It is the reaction of a normal but high strung child to these stimuli. While these things cannot be entirely overcome, many terrors can be eliminated by proper premedication.

Contrary to what some of us were taught, children take morphine quite well, and in relatively large dosage. Dr. Robson, of Toronto, whose experience has been large as enesthetist to the Hospital for Sick Children, gives the safe dosage as the fraction of a grain represented by the age over 60. He routinely premedicates his children.

Dr. B. C. Leech, of Regina, Saskatchewan, Canada, gives the following premedication to children coming up for operations, including tonsil and adenoid removal:

Age	Morphine	Hyoscine
6 mos. to 1 year		1/900
1 to 2 years	1/40	1/900
2 to 4 years	1/32	1/600
4 to 8 years	1/20	1/600
8 to 12 years	1/16	1/450
12 to 16 years	1/12	1/300

He found that this combination was much more consistent in its action than the barbiturates. The head pediatrician in charge of the wards and the head nurse who had been on these wards for years, were both quite enthusiastic in their commendation of this method of premedication as compared with their experience when no premedication was given. In addition to the dose of morphine and scopolamine we give a small dose of a short-acting barbiturate to larger children. When given alone Leech found that the barbiturates were inconsistent. In combination with the hypodermic medication we like them.

Barbiturates, tribromethyl alcohol or paraldehyde can be used in adults in addition to a dose of morphine and scopolamine. We find that a moderate dose of a briefly acting barbiturate, orally, in addition to the morphine and scopolamine, works well. Generally speaking, patients with high metabolic rates require larger amounts of premedicaments.

Never commence the administration of an anesthetic without inspecting the equipment and seeing that it is complete: sufficient anesthetic agents, air ways, lubricant, and a laryngoscope that works. It is unpardonable, and most inconvenient and disconcerting, to need some little part of the equipment, such as an air way or a connection, or to find that the laryngoscope does not work, or that the air way needed for the particular case cannot be found, or that the supply of gas is inadequate. It is possible that the ether machine for tonsillectomies has been connected backward by the nurse, and a stream of ether may be sprayed over the face. Without first inspecting I have turned on the machine, with the ether tip hanging in the mouth, and shot a stream of ether into the throat. Never fail to inspect this.

When the patient is brought to the operating room, every effort should be made to avoid excitement. The talking of nurses or other attendants, the rattling of pans, and so on, should be stopped. The restraining strap above the knees should be applied so loosely that the patient will not notice it, but should be arranged so that it can be tightened immediately. Its use is seldom needed. If the patient is still conscious, the anesthetist should walk around where he can be seen by him, and speak a few cheerful words. Do not wear a mask at this stage. Then, while adjusting the blood pressure cuff and stethoscope to the arm, reassure him with cheerful comments. Place the restraining halter under the head. With a reassuring pat on the cheek, carefully fit the mask to the face, but do not fasten the halter at this stage. Do not remove full plates, as they are very useful in supporting the jaw. Now begin the induction in the way that, in your hands, has proven most satisfactory. Do not move or handle the patient during induction. Everyone should be quiet and only the anesthetist should talk to the patient if any talking is done. Many patients like to hold a hand during induction. The hand held should not be a hurried one, the patient being allowed to hold it until he is unconscious. A gentle pat and slight squeeze has its psychologic effect on nervous patients. Some do not want to be touched. Do not touch them.

Since the prime object of this paper is not the actual technic of induction, only a few remarks will be made regarding that.

In using the closed carbon dioxide method of anesthesia, it must be borne in mind that it takes some little time to eliminate the air, with its large percentage of nitrogen, from the lungs and

blood. If this is not done before rebreathing technic is instituted, anesthesia will be unsatisfactory when nitrous oxide or ethylene is used. With either ethylene or cyclopropane there is seldom a stage of struggling or excitement. This incidence is much higher with nitrous oxide.

When cyclopropane is the agent used the elimination of all the air is not important, for quite a bit of nitrogen in the anesthetic mixture will not interfere with the anesthesia. It is also possible, and sometimes desirable, to add a lighter than air agent, like hydrogen or helium, to the mixture. In this case the air should be replaced by pure oxygen in the beginning, then a mixture of helium or hydrogen and cyclopropane, together with a metabolic flow of oxygen, should be added to the bag. The rate of flow of the two light gases, when an oxygen or carbon dioxide flow meter is used, will be about three times the reading on the flow meter. These light gases have a tendency to leak out of the system.

Avoidance of laryngeal spasm is important. We have found that the incidence of spasm during induction is smaller if, in the building up of the percentage of cyclopropane to the required amount for the case, its flow is slow at first; second, if no attempt is made to do anything to the patient until he is well under; and third, if the carbon dioxide absorber is switched off during induction. After induction of anesthesia the carbon dioxide absorber is switched on. For a period of several minutes following this a small flow of 100 c. c. of cyclopropane is continued to compensate for the gas absorbed by the tissues.

SUMMARY

(1) Every patient should be seen by the anesthetist before the time for induction of anesthesia, if possible.

(2) The impression made by the first contact of the anesthetist with the patient should be such as to inspire perfect confidence.

(3) Premedication is very desirable in almost all cases.

(4) Quiet should prevail at the time of actual induction.

(5) An unhurried induction is best.

1640 Robert Street

DISCUSSION (*Abstract*)

Dr. Lucy S. Hill, New Orleans, La.—Self-confidence on the part of the anesthetist is absolutely necessary in order that the patient's confidence may be maintained. The movements of the anesthetist must be swift without appearing to be hasty or due to lack of familiarity with the usual routine. Talking or laughing on the part of the anesthetist or other persons in the operating room should be avoided, as this gives the patient the impression that his operation and anesthesia are considered unimportant and are not receiving the consideration which he deems important for the continuation of his existence.

As regards the various agents used in the induction of anesthesia, I might stress the comfort and ease with which cyclopropane may be used. There is rapid induction and absence of disagreeable sensations such as may be caused by oxygen deficiency and the unpleasant odor which we associate with ethylene or ether. The patient very quickly passes into the stage of surgical anesthesia desired and transition to ether, as in tonsillectomy cases, is very easily and quickly accomplished.

It is through the untiring efforts, the enthusiasm and ability of Dr. Caine that anesthesia is maintained upon its present high plane in New Orleans, and it is through his influence and worthy example that many capable physicians have become interested in anesthesia and are devoting time and energy to it.

LONG LABORS: THEIR CAUSES AND CORRECTION*

By W. T. Pride, M.D.
Memphis, Tennessee

Not until recent decades have obstetricians taken an active interest in the causes and measures for correction of long labors. Indeed, it has been less than a century since attempts to relieve the suffering of women in childbirth were discouraged as being contrary to biblical teaching. Since the beginning of the present century, however, progress in this phase of obstetrical practice has been phenomenal. We are now able to say with some certainty what these causes are, and, although no infallible rule has been worked out for their correction, the procedures of current practice may, when properly carried out, be relied upon to obviate an untold amount of suffering and save countless mothers and babies from injury, and even death.

The principal causes of long labor may be enumerated as follows:

(1) Inertia uteri
(2) Pelvic tumors
(3) Deformities of the pelvis
(4) Disproportion between the size of the passage and passenger
(5) Deformities of the fetus
(6) Malposition of the fetus
(7) Retraction rings

The first of these, inertia uteri, or a sudden

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cessation of uterine contractions, is encountered chiefly in multiparas. Often, it occurs without any apparent reason, although it may be occasioned by malposition of the fetus. Examination may disclose full dilatation with the head in the middle or low pelvis. Usually, delivery can be effected by giving the patient 3 minims of posterior pituitary extract hypodermically or 10 minims on cotton intranasally, and breaking the water. If this does not suffice, one must resort to forceps manipulation or podalic version.

Tumors, deformities, disproportion and malposition should be discovered as soon as possible, and at least before labor begins. At the patient's first visit in pregnancy pelvic measurements should be taken to determine the size of the passage, that the weight of the fetus may be controlled accordingly by diet and hygiene. Pelvic examination should also include an investigation of the size and position of the organs and a search for abnormalities. As term approaches, invariably a roentgenogram should be made to demonstrate the size of the infant and its position, as well as any deformities of the fetus or pelvis. By these means, one can be forewarned of any untoward developments and be prepared to guard against them.

When confronted with the possibility of a long labor, one's first thought should be to induce complete analgesia and relaxation. This, of course, is true in every case, but especially so when there are complications which tend to prolong labor unduly and invite grave danger.

As soon as the patient in labor enters the hospital, following the usual preparations, she is examined both abdominally and vaginally. She then receives a rectal injection of 3 to 6 grains of one of the barbiturates. This should induce sleep until the pains become severe. When she awakens and begins to complain, morphine sulphate gr. 1/6, and scopolamine gr. 1/200 are given by hypodermic. A smaller portion of this dosage, alternating with 1½ to 3 grains of one of the barbiturates combined with scopolamine gr. 1/300, is administered thereafter as necessary. If these analgesics are not efficient, 30 c. c. of paraldehyde may be given per rectum. By this technic, the patient should be kept fairly comfortable, labor should be shortened, and no harm should accrue to the baby.

Another important point in preventive treatment is the feeding of the patient. In severe labors, the normal chemistry of the blood usually is altered, the carbon dioxide combining power is reduced, and acidosis, or, rarely, alkalosis supervenes. To obviate these developments, patients should be fed and given an abundant quantity of fluids, while the anesthesia is continued.

Several years ago, in the department for teaching of the University of Tennessee, we observed that a number of ward patients on our service, after being in labor for more than eighteen hours, suffered shock, and a few succumbed suddenly to the anesthetic. To our surprise, we discovered that the anesthetist had ordered that they be given nothing by mouth during the second stage of labor, in order to prevent nausea in anesthesia. The carbon dioxide combining power of the blood of these patients was found to be excessively low.

This discovery inspired us to carry out some experiments at the University to learn what happens in the body during long labor. Our first studies were made upon dogs. A number were purged and starved until they were in a state of profound acidosis, then were given an anesthetic of ether, chloroform, or gas. Almost every one of these dogs died. Others, to which an intravenous injection of sodium bicarbonate had been given prior to the anesthetic, apparently suffered no ill effect. Occasionally an acidosis was produced by an intravenous dose of 2 per cent lactic acid. Thereafter, we estimated the carbon dioxide content of the blood of all patients in long labor and found that almost invariably an acidosis existed. If the patients were fed and given fluids during labor, however, the carbon dioxide content remained approximately normal.

As has been stated, abnormalities in either mother or child may be, and generally are, responsible for the most common of the causes of long labor: malposition of the fetus. By far the most prevalent of the positions which the obstetrician is called upon to correct is the occiput posterior presentation. As a matter of fact, this has come to be an almost daily experience; roentgenograms of 800 of the author's private patients made during the past few years have shown an occiput posterior position of the fetus in 70.6 per cent.

Of course, if labor is allowed to progress without interference until the caput is at the perineum, the resistance encountered at the pelvic floor will serve to effect rotation in many cases, but this is accomplished at the expense of great danger to the child and an unnecessarily long period of suffering for the mother. No doubt, many infants die and mothers are injured from unassisted occiput posterior deliveries, and, even though the baby survives and the mother is not permanently injured, the morbidity is excessive

because of the long labor, and the consequent exhaustion and frequent infections.

Manipulation may be undertaken when analgesia is complete and dilatation fairly well advanced; one need not wait for complete dilatation, as this is always slow in posterior presentations. The patient is then placed upon the delivery table and given gas with each pain. The perineum is dilated and a catheterization is done. Then, with each hard pain, the index finger is pressed gently against the anterior occipitoparietal suture. This gives the necessary resistance and, with a very few pains, the desired result should be accomplished. If this procedure is not sufficient, however, midforceps are applied, the handles depressed, and the head pushed up very gently and turned right or left, depending upon the direction of the fetal back. The head then comes down in the anterior position, forceps are reapplied, and delivery is completed.

Should the head fail to descend far enough to permit the carrying out of this method, a podalic version should be employed. The success of the version will depend upon the size of the passage and whether relaxation is complete. It also calls for the exercise of sound judgment and expert manipulation.

Although breech presentations are familiar to all, since they are not seen in every-day practice, a mastery of the technic of delivery is difficult to acquire. The frank breech is the type commonly observed. The cervix usually dilates quickly, but expulsion proceeds slowly, and it is advisable to deliver the baby when dilatation is complete. Under deep anesthesia the hand and arm are inserted into the uterus, as for podalic version, the ankles of the baby are grasped, the legs bent at the knees, and the feet are brought down through the vaginal opening, thus converting the breech to a footling. By this technic one has complete control of the position of the head for extraction.

Occasionally we find the body of the fetus lying in the transverse position. If this is discovered before labor begins, it may be corrected by abdominal manipulation, although extreme care should be exercised to avoid premature separation of the placenta. If no correction has been made, a podalic version should be done when dilatation is complete. Should dilatation fail to take place, a cesarean section is indicated to prevent rupture of the uterus.

Another malposition rarely observed is that in which the shoulder is presented, perhaps accompanied by a prolapsed arm. If the shoulder alone is presenting, after complete dilatation the patient is given a general anesthetic, the shoulder is pushed up, and a podalic version done. If the arm is prolapsed, extreme precautions should be taken against infection before manipulation is attempted. The arm should be bathed in tincture of green soap, dried, and a 10 per cent solution of mercurochrome applied. A small quantity of mercurochrome should also be injected into the vagina. After full dilatation of the vagina, the arm is replaced and a podalic version done. Here, also, one needs to exercise particular care in manipulation to avoid rupture of the uterus.

We come now to the last of the causes of prolonged labor. This is the retraction ring. In reality, this is an effect as well as a cause. It occurs in labors already prolonged by any of the factors enumerated, particularly disproportion and malposition, and is induced in part by their sequel, an unbalanced chemical content of the blood. Early rupture of the membranes may also contribute to its development.

The retraction ring serves further to prolong labor and, if not corrected, leads to tetany uteri and the necessity for cesarean section.

The mechanism of the retraction ring has its basis in the anatomic distribution of the muscular fibers of the uterus. These fibers are arranged in three layers. In the outermost layer they run principally in a longitudinal direction; in the middle layer, radially; and in the innermost layer, in an oblique and circular direction. Within the innermost layer, at a point just above the internal os, is a thicker segment of annular fibers, and it is at this point that the retraction ring occurs. The waves of contraction which sweep over the uterus during parturition begin at the fundus and involve, for the most part, the three layers, continuing to do so until the uterine contents engage the cervix; the circular fibers then contract more vigorously in the wake of the fetus. Normally, the circular contractions produce rings of constriction which are alternately loosened by the retraction of the longitudinal fibers. By this combined effort, the fetus is pushed toward the outlet, while coincidentally the uterine rings are pulled back and slipped over the fetus.

It is conceivable that failure of the longitudinal fibers to loosen these rings of constriction can throw the entire uterus into a state of contraction, thus preventing its contents from moving outward. Constrictions of this type may occur at any point. They are initiated by some of the same factors which produce retraction rings, but

may be easily relaxed by mild analgesia and anesthesia. However, when the longitudinal fibers fail to loosen the circular fibers composing the annular segment of the innermost layer, which is known as the physiologic retraction ring, the other layers are engaged in the constriction, the ring becomes thickened and rigid, causing obstruction, the cervix relaxes, the uterus above the ring becomes tense, and the abdomen is painful upon pressure. The physiologic retraction ring thus becomes pathologic.

This pathologic ring may obstruct with varying degrees of force. In the most severe form, every muscle fiber of the uterus is contracted and retracted, allowing no relaxation and producing in the uterus a condition of tetany. The tenseness may be so acute and so forceful as to compress the blood vessels supplying the fetus and lead to its asphyxiation. Occasionally, one sees a rupture of the lower uterine segment from over-stretching and thinning of the walls.

In making a diagnosis of retraction ring, one may be guided by the following signs:

(1) Prolonged labor; that is, from twelve to thirty-six hours.

(2) Malposition and slight advancement of the fetus, the head or presenting part within the dilated cervix.

(3) The appearance of a sulcus across the lower abdomen above the symphysis pubis, at a level corresponding to the peritoneal attachment where the coronary vein crosses the body of the uterus.

(4) Tenseness of the uterine body above the sulcus and pain on palpation of the abdomen.

(5) On vaginal examination, a freely movable presenting part, and a cervix dilated sufficiently to permit the passage of the examining hand beyond the portion where the ring is found.

(6) A low carbon dioxide combining power of the blood.

Treatment is both preventive and curative. Preventive measures consist of the institution of complete analgesia to promote relaxation and the administration of abundant fluids to maintain a normal chemical ratio of the blood. If, in spite of these measures, a ring develops, or is already present when the patient is examined, a test is made for the carbon dioxide combining power of the blood. When this is found to be low, an intravenous injection of 1 to 2 per cent sodium bicarbonate is given. The analgesia is continued. If the ring persists when the patient is ready for delivery, 6 minims of epinephrine solution are given hypodermically to obtain relaxation and ether is administered. It is essential that both analgesia and anesthesia be allowed to take full effect before an attempt is made to deliver.

The use of mid or low forceps according to the method described is the most suitable procedure for delivery. Podalic version involves serious danger in a tense uterus and should be avoided when possible. If the analgesics, sodium bicarbonate, epinephrine and anesthetic fail to relax the uterine retraction, tetany develops, and the baby shows signs of distress, a cesarean section should be performed.

In conclusion, I should like to say again that the most important one factor in the management of labor is the institution of proper analgesia. Upon this measure alone depends the larger portion of our success. Not only does adequate analgesia render the patient insensible to her suffering, but, by promoting more rapid dilatation and relaxation, it shortens labor and permits greater ease and facility of delivery.

Today, approximately one woman in ten goes through labor without the benefit of analgesia. Surely, this is an indictment of our profession. We can no longer sit idly by and console ourselves with the thought that to alleviate the pain of childbirth is contrary to the precepts of the Bible; no one will deny that such theories belong to the Dark Ages. Nor can we say that the baby will suffer any harm. The proper application of our present knowledge should entail no danger to the life or well being of the infant from analgesia. We can, in fact, find no excuse for neglecting our obligation, for contenting ourselves in ignorance and indifference.

We need only be diligent in study and research in this field. By a familiarity with measures now at our disposal, we should be able to control the progress of every labor, reducing materially the duration of even those which are complicated, eliminating many of the hazards to both mother and child, and minimizing the need for drastic methods of correction.

DISCUSSION (*Abstract*)

Dr. W. B. Anderson, Nashville, Tenn.—It is refreshing to see a man like Dr. Pride take up the most common place incidents in obstetrics and comment on them in an intelligent way. Obstetrics has made wonderful progress in the last half century and yet maternal and infant mortality has not been materially reduced. I am reminded of the saying of an old Tennessee doctor: "It is better to recede than persist in error. It is possible

to advance faster and further than sound philosophy guides. Not all that is new is good and likewise not all that is good is new." Dr. Pride's paper is splendid and upon the whole very practical, but I must disagree with him in some instances.

It is not practical to get too routine. Each pregnancy has its own individual problems.

I do not think it always necessary or practical to make an x-ray picture to demonstrate a position or presentation. And I think that pelvimetry is usually sufficient for the average pelvic problem. A physical examination will demonstrate the average disproportion or deformity. If disproportion is present a roentgenogram is of great help to decide what course to take or how to proceed. As Dr. Pride says, the majority of babies, *in utero,* lie cccipito-posterior until engagement takes place. About 70 per cent of them will rotate to an anterior position by the time dilatation is complete and 96 per cent of them will eventually rotate if let alone.

In normal obstetrics we know that the average time of a primiparous labor is eighteen hours, and many labors may be longer and yet normal. Most of this time is taken up in first-stage labor. Except with rare indications, interference to shorten first-stage labor manually can only be classed as accouchement force, that breeds trouble. A manual rotation, and especially a forceps rotation, call for complete dilatation. And many times a version is preferable.

Analgesia in obstetrics is here to stay, and is a great boon to suffering humanity. Every woman in labor should have the benefit of some of the many agents used for this purpose. The physician should use the agent he is best acquainted with. In the average case I use sodium iso-amylethyl barbiturate in the beginning of labor; morphine and scopolamine when labor is established, and rectal analgesia (Gwathmey method) in the beginning of the second stage, followed usually with ether or gas anesthesia. I believe, when properly used, it shortens labor and helps to prevent a Bandl's ring. I have not seen a Bandl's ring after proper use of analgesia.

The time to feed a patient properly is before she goes into labor. After she goes into labor, she does not digest her food well, and the anesthetist may be right. Frequently the content of a stomach full of undigested food is vomited. Undigested food does not prevent acidosis. I prefer giving 1,000 c. c. of 10 per cent glucose intravenously during labor or just after delivery. There are many points in Dr. Pride's excellent paper to discuss. I will only say, individualize your patients and do not get too officious.

Dr. James R. Garber, Birmingham, Ala.—In my own mind, I make a differentiation between the retraction or Bandl's ring and the constriction ring. The former is found high up in the uterus, while the latter is just above the internal os. In two cases I did insert a bag and secured complete dilatation. I put a bag in the constriction ring case.

Dr. Pride (closing)—I do not understand Dr. Garber's procedure. He stated he had placed a 22 centimeter bag in a case of retraction ring. Dr. Garber's idea of the ring is entirely different from mine.

The ring is tight around the baby's neck and the uterine body above is very tense. It would be impossible to insert the bag, but if perchance one could insert it, if filled with water the uterus would rupture.

INDICATIONS, TECHNIC, AND COMPARATIVE EVALUATION OF INJECTION AND OPERATIVE TREATMENT OF HEMORRHOIDS*

By MARION C. PRUITT
M.D., F.A.C.S., F.R.C.S. (ED.)
Atlanta, Georgia

The common conditions that are amenable to treatment but often neglected are most interesting to me. Hemorrhoids, the most common of all anorectal diseases, are in this group.

For an understanding of this subject a brief review of the anatomy of the parts is essential.

The terminal portion of the alimentary tract in the order met with during proctoscopic examination is the anus and rectum.

The anus is ectodermal in origin, formed from the proctodeum, and is that portion of the alimentary tract which extends from the margin of the true perianal skin to the pectinate line or the mucocutaneous junction. The anus is about one-half to three-fourths inch in length and forms the lower part of the anal canal.

The rectum is entodermal in origin and is formed from the hindgut. It is that portion of the intestinal tract which extends from the mucocutaneous junction or pectinate line to a level opposite the third sacral vertebra. The rectum is five to seven inches in length and is continuous with the sigmoid above.

The proctodeum as it develops to form the anus invaginates inward and upward to meet the blind end of the hindgut and carries with it its blood, nerve and lymphatic supply. The hindgut as it develops to form the rectum passes downward and brings with it its blood, nerve, and lymphatic supply. In its downward descent to meet the blind end of the proctodeum it passes through the pelvic fascia, carrying down on its wall a tubular prolongation of this fascia. The developmental processes bring together the blind ends of the proctodeum and hindgut, or the epiblastic and hypoblastic primary germ layers. The fusion and absorption of the blind ends complete the terminal opening of the alimentary tract.

The line of fusion of the proctodeum and hindgut or of the anus and rectum forms the mucocutaneous junction or the pectinate line

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and is the dividing line between the superior hemorrhoidal vessels above and the inferior hemorrhoidal vessels below. This is the anatomic reason for the two distinct varieties of hemorrhoids, external and internal. The external hemorrhoids implicate the inferior hemorrhoidal veins and the internal hemorrhoids implicate the superior hemorrhoidal veins.

This developmental process of the nerve supply explains the cause and character of pain according to anatomic location of the lesion, as below this line the anus and external sphincter muscle are richly supplied by sensory nerves from below. Above this line, the rectum and the internal sphincter muscle are supplied by the sympathetic nervous system from above, like the other portions of the alimentary tract. Therefore, lesions, injuries and pathologic conditions below the pectinate line may give rise to extreme pain, particularly the ones within the grasp of the external sphincter muscle. Lesions, injuries or pathologic conditions above the pectinate line give little or no pain except tension pain, or a feeling of fullness or pressure.

Hemorrhoids may be defined as swellings or masses which originate in a dilatation or varicosity of one or more groups of the veins of the anus and lower rectum. The masses may be outside of the rectum, they may be inside, they may be inside and protrude outside, or they may be both inside and outside. They often bleed and protrude during defecation and they tend to result in thrombosis and interstitial fibrosis.

Hemorrhoids are classified anatomically in two varieties, external and internal, depending upon whether the veins from which they originate are situated below or above the pectinate line. Thus: external hemorrhoids implicate the inferior and middle hemorrhoidal veins and are covered solely by skin. Internal hemorrhoids implicate the superior hemorrhoidal veins and are covered solely by mucous membrane.

There is a definite communication between the inferior and the superior hemorrhoidal veins which extend around the anal canal at the mucocutaneous junction. Any condition that causes dilatation of one set of these veins necessarily must through their communication be felt in the other set. This anatomic fact accounts for the frequent occurrence of both external and internal hemorrhoids in the same patient. Each variety may occur as a separate condition. If both varieties appear combined they are designated as combined, externo-internal or mixed hemorrhoids.

The anatomic divisions are further classified as the simple and complicated.

The complications of external hemorrhoids are: thrombosis, rupture, fibrosis or skin tabs, and inflammation.

The complications of internal hemorrhoids are: thrombosis, strangulation, gangrene, and inflammation.

The common symptoms of hemorrhoids are: bleeding, protruding, swelling, pain, feeling of fullness or discomfort, tenesmus, sphincter spasm, itching and discharge.

Symptoms less commonly recognized as being due to piles are: nervousness, low blood pressure, low backache, urinary disorders, digestive disturbances, anemia, headache, insomnia, sciatica, "gas," and menstrual disturbances.

While no one of these symptoms is diagnostic, any one of them demands a careful proctosigmoidoscopic examination to rule out hemorrhoids or to diagnose other associated or complicating lesions.

The following conditions may be mistaken for hemorrhoids: marginal, submucous, ischiorectal and pelvi-rectal abscesses, prolapse of the rectum, hypertrophied anal papilla, condylomas, anal warts, lymphopathia venerea, fissure with sentinel pile of Brodie, benign tumors, epithelioma, adenocarcinoma, and intussusception. These conditions should be ruled out by careful examination and should be considered as a separate entity even though they are associated or complicated with hemorrhoids.

It is not today the question of whether piles can be cured by palliative, electric, injection or operative treatment. The questions are, what is the comparative value of the various methods and is one method more suitable for a certain kind of case than another?

The fact that there is lack of agreement as to the answer to these questions is common knowledge. This is partly because comparative data are unavailable. Comparative evaluation and choice of method can come only from one who has had considerable experience in the use of all of them. The enthusiasm of one who uses only one method is of little value. Criticism of method because of certain abuse or secrecy of use by unscrupulous practitioners does not indicate or determine its value. Statements of high pressure salesmen representing manufacturers are often exaggerated. While every encouragement should be given to the development of auxiliary aids, their value should be determined by a scientific comparison of the results obtained

through the use of these aids and the results of the accepted methods.

The choice of method may depend on the local lesion or the condition of the patient. Thus, as a rule, acutely inflamed hemorrhoids are best handled by palliative methods until the inflammatory process subsides.

Irreducible strangulated thrombosed internal hemorrhoids with a relaxed sphincter, in my experience, are best treated by palliative measures until the swelling of the protruding parts recedes. This is especially true when complicated by acute infection. Cases with constriction of protruding parts, due to a contracted sphincter, sufficient to produce sloughing or gangrene of the parts, demand an emergency operation. Some surgeons hold that all cases of irreducible strangulated thrombosed internal hemorrhoids demand immediate operation.

Hemorrhoids complicated by constriction of the anus, fissure-in-ano, fistula, hypertrophied papillae, chronic cryptitis or thrombosed external hemorrhoids are surgical.

Simple internal hemorrhoids without local complications are suitable for either injection or operation. In many cases the choice of the patient may be the deciding factor.

Combined external and internal hemorrhoids are surgical if a cure is to be expected.

Hemorrhoids become a secondary consideration when associated with cancer of the rectum.

In cases of secondary anemia with hemoglobin of 40 per cent or lower due to the loss of blood from internal hemorrhoids or in cases of delayed clotting time, injection treatment for the control of hemorrhage is the method of choice until the improved condition of the patient will permit further injection or operation.

Patients with hemophilia or purpura are poor surgical risks; hemorrhage following operation may prove fatal. When the bleeding from internal hemorrhoids is sufficient to demand surgical measures for the control of hemorrhage, the injection treatment, using the smallest needle possible to carry the solution, injecting into the center of the hemorrhoid just enough of a weak solution to control the hemorrhage, is the safest and simplest method.

Patients with congestive heart failure or renal insufficiency, advanced tuberculosis or diabetes, and old people whose life expectancy is short, are more safely treated by injection. The injection treatment can be given with little discomfort and practically no reaction, but with immediate relief of symptoms. In some cases the treatment should not be carried further than the relief of symptoms. If operation is preferred in such cases, local anesthesia should be employed.

INJECTION TREATMENT

The kind and strength of the solution, the amount to be injected, and the point or method of injection are matters upon which difference of opinion exist.

There are two more or less standard solutions: carbolic acid varying in strength from 5 to 20 per cent, suspended in glycerine and water or vegetable oil; and quinine urea hydrochloride 3 to 10 per cent in aqueous solution. Various other solutions have been advocated.

If carbolic acid (5 to 12 per cent) is to be used and the injection is to be made into the center of the hemorrhoidal mass, glycerine and water are the vehicle of choice and the amount to be injected into each hemorrhoid is to be measured in drops (3 to 10 minims). If the injection is to be submucous, a vegetable oil is the preferred vehicle and the amount to be injected is more and is to be measured in cubic centimeters (1 to 6 c. c.).

Whatever formula is used, the object of the injection treatment is to produce by irritation with a chemical solution sufficient fibrosis to obliterate the network of dilated veins forming the hemorrhoidal mass, thus causing it to shrink, but not sufficiently to cause sloughing of the tissue. It is better to inject too little solution than too much, as too large an injection predisposes to sloughing.

Only simple internal hemorrhoids without complications are suitable for the injection treatment.

OPERATIVE METHODS

The operative methods that have received general recognition are: excision and suture, ligation, clamp and cautery, and Whitehead's. Although there are various modifications of these operations, the essentials of each have been changed very little. The principal differences are the excision of redundant skin, the method of suturing, the placing of clamps, some special kind of forceps, or other slight variations of technic. Whatever operation is to be done, a relaxed sphincter is essential.

There is no question in my mind about the superiority of the excision and suture operation for neatness, accuracy, control of hemorrhage, postoperative discomfort, and ultimate results. It approaches the ideal of our present surgical teaching. The following modification with

slight variations to meet the needs of the individual case has been most satisfactory in my experience.

Author's Method of Excision and Suture.—The sphincter is gently dilated to bring the piles well into view. If the sphincter is relaxed, no dilatation is necessary. The anal margin is grasped at equidistant points with Pennington's triangular forceps and traction is made outward. This everts the anus and brings the hemorrhoids well into view.

The most important portion of the pile is grasped with a Pennington's forceps and pulled down. An incision through the excessive cutaneous structures is made around the margin of the pile on to the mucous membrane.

A hemorrhoidal clamp is applied in the groove in the long axis of the bowel at a sufficient depth to include all of the hemorrhoidal tissue, and clamped tight to prevent slipping. A No. 1 plain catgut ligature on a round curved needle is then placed through the mucous membrane and around the blood vessels at the upper pole of the pile above the end of the forceps, and tied. This suture is to cut off the blood supply of the pile from the superior hemorrhoidal vessels. One end of the same suture is continued as an over-and-over suture around the forceps through the base of the pile in the line of the incision. This part of the suture includes the mucous membrane, but does not include the skin. It emerges in the groove just beneath the cut edges of the skin. Then the loops of the over-and-over suture are pulled over the end of the forceps to avoid being cut, and the portion of the pile distal to the clamp is trimmed away. The loops of the suture are now replaced over the forceps and gently pulled down around the forceps. The forceps is then removed, the loops are drawn tight, and the two ends of the ligature are tied.

Any excessive, redundant, irregular perianal skin folds are trimmed away so as to leave a V-shaped point extending out on the perianal skin to make it smooth and to facilitate drainage. Judgment is required as to the amount of redundant skin to be trimmed away, as the part should be smooth and without constriction when it heals. Bleeding from external vessels is rarely sufficient to require clamp and twisting or suture.

The finger is inserted into the rectum and if there is any narrowing caused by the ligatures and suturing of the piles, it should be stretched until there is no constriction.

The operation is completed by inserting into the anal canal one end of a small wick of sterile gauze which is covered with a local anesthetic ointment. The other end of the wick is fluffed over the anal orifice; over this is placed a sanitary pad which is held firmly in place by pinning it in front and back to a bandage around the waist (T-binder). At the end of twenty-four hours the wick of gauze is removed from the anal canal.

The suture placed above the end of the forceps ligates the superior hemorrhoidal vessels which enter at the upper pole of the pile and prevents hemorrhage. The over-and-over suture closes the wound as a continuous suture. This method of suturing does not include the skin which is richly supplied with sensory nerves, and therefore minimizes postoperative discomfort. The over-and-over sutures around the forceps through the stump are placed before the cutting away of the pile to avoid the possibility of a portion of the stump's slipping from the grasp of the hemorrhoid forceps, which might cause hemorrhage.

COMPARATIVE EVALUATION OF INJECTION AND OPERATION

Recently Kilbourne compiled from a questionnaire to 293 outstanding proctologists in the world comparative statistics as to the value of methods of treatment in 59,633 cases of internal hemorrhoids.

26,183 cases were treated by injection.
33,450 cases were treated by operation.

Of the operative cases the types of operations used were:

Ligature and excision	25,293 cases
Clamp and excision	2,584 cases
Cautery	5,467 cases
Cautery and suture	250 cases
High frequency	150 cases

To summarize, 60 per cent were treated by operation, 40 per cent by injection, and only 0.2 per cent were treated by electric methods.

Hemorrhage occurred after treatment as follows:

Operation	0.573 per cent
Injection	0.279 per cent

Stricture occurred after treatment as follows:

Operation	0.2 per cent
Injection	none

"Recurrence of the hemorrhoids was much more frequent after the use of injection methods, occurring probably in at least 15 per cent within three years."

The advantages of the injection treatment are

that it is practically painless and it is an office procedure, not requiring hospitalization or financial loss in absence from work. The injection treatment in many cases gives the patient what he demands. Recurrences are partly due to insufficient treatment and when they do occur it is a simple matter to give further injections. It must be remembered that injection treatment is suitable only for internal hemorrhoids without local complication.

The advantage of operative treatment is that it is suitable for both external and internal piles. It allows for the removal or drainage of other local diseased conditions which are commonly associated with hemorrhoids and the results are more permanent.

In the hands of experienced men a cure of uncomplicated internal hemorrhoids is to be expected in 80 to 85 per cent when treated by injection and 90 to 95 per cent when treated by operation.

REVIEW OF METABOLIC AND CLINICAL STUDIES IN AMINO ACID THERAPY*

By CARLO J. TRIPOLI, M.D.
and
HOWARD H. BEARD, PH.D.
New Orleans, Louisiana

Since the publications of Milhorat, Techner and Thomas[1] on the beneficial effect of amino acid therapy in pseudohypertrophic muscular dystrophy, many reports have appeared. The different types of therapy advocated and the divergence of clinical results reported have only served to cast doubt upon the proposed efficacy of any one of them. In previous reports,[2 3] studies of several phases of this problem have been presented. Particularly striking were the metabolic changes observed in the patients studied, but equally impressive were the variations in end clinical results.[4] Of great importance, naturally, is the permanence of the beneficial results following amino acid therapy and whether or not such treatment can be considered only as a "substitution" form of therapy, like insulin, and therefore must be continued throughout the life of the patient.

CREATINE-CREATININE METABOLISM

Since the time of Aran[5] and Charcot,[6] researches into the etiologic factors and pathological lesions of the myopathies have been pursued with diligence. The discovery of the role played by creatine, as phosphocreatine, in muscular contraction, by Lundsgaard[7] and others, served again to focus attention of biochemists upon the origin of muscle creatine in both normal and myopathic individuals. Hunter's monograph lists several studies showing the exogenous origin of creatine. In 1919, Levene and Kristeller[9] demonstrated the exogenous origin of creatine by feeding proteins to muscular dystrophy patients. Much interest in this question was again aroused by the results of the studies of Brand, Harris, Sandberg and Ringer,[10] who showed that amino acid feeding to this type of patient resulted in an increase of 40 per cent in creatine excretion in the urine. Beard and co-workers[11 12 13] show that the feeding or injection of suitable doses of many different amino acids and related substances caused an increase in muscle creatine and an increase in creatine excretion. Similar results were obtained after injecting small doses of the methylated purines and prostigmin.* [15 16]

A number of investigators[1 17-23] have published similar results on creatine formation and excretion when arginine, glycine, glycocyamine and caffein were fed or injected. This evidence shows the importance of the methylation process in the body on creatine formation. However, the possibility of increasing muscle creatine by other factors still remains to be shown.

Creatine is usually not excreted in the urine of adult men, but women and children may eliminate a small amount, which is considered physiological. Creatinuria is not only present in cases of pseudohypertrophic muscular dystrophy, but also in progressive muscular dystrophy,[1 10 17 24 25 26] amyotrophic lateral sclerosis and acute anterior poliomyelitis,[1 2 27] and myasthenia gravis.[28]

Many of these investigators observed that not only is there an initial creatinuria, but a definite increase in this creatine excretion following amino acid therapy. With continuation of this therapy, the increased creatinuria soon

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*From the Departments of Medicine and Biochemistry, Louisiana State University Medical Center, and the State Charity Hospital, New Orleans.

*Using the creatinine enzyme of Miller and Dubos,[14] it was shown that the color of the Jaffe reaction in these experiments was specific for creatinine.

diminishes to that of the initial level and often becomes minimal. In general, those patients in whom this increase and decrease was noted showed the most marked improvement. The method of study in our cases, together with a tabulation of the initial metabolic studies and clinical results, has been previously reported.[2 4]

We have endeavored to observe our patients over a sufficient length of time to elucidate some of the complex problems presented and perhaps be able to suggest the role played by other factors in various myopathic diseases. We have been able to do the initial and subsequent creatine-creatinine studies in 51 cases representing 12 different types of myopathies; 38 of these have been observed over a period of 4 years, and the others for a shorter period of time. The cases were classified on a pathological-clinical basis rather than as eponymic entities.[2]

CLINICAL OBSERVATIONS

The criteria for improvement in the patients were arbitrarily based on (1) the ability to perform the usual coordinated daily routine tasks of normal individuals, (2) the strength or lifting power of certain muscles or groups of muscles, (3) the number of times the muscles were able to contract against a load before complete fatigue resulted, and (4) the length of time fatigue lasted before recovery of the muscle was complete. These criteria have been insisted upon in each case and had to be fulfilled before classification of the result was noted. The majority of cases showed considerable subjective improvement which was disregarded in order to eliminate the psychic effects prominent with many types of therapy.

Table 1 shows a group of 14 cases of various myopathies in which both subjective and objective improvement could be definitely demonstrated over a period of several months to two years. Of the 12 different clinical conditions studied, the only ones showing initial improvement were those of progressive muscular dystrophy, pseudohypertrophic muscular dystrophy, paramyoclonus multiplex, myasthenia gravis with and without strabismus, and diplopia. One case of early spinomuscular atrophy had a remission which may possibly be coincidental and not due to the amino acid.

*Table 2** shows the results in the same 14

*The case numbers are the ones originally given in our previous publications.[2 3]

Table 1

CASES IN WHICH OBJECTIVE IMPROVEMENT WAS OBSERVED

Case No.	Age	Amino Acid 10-20 gms.	Urine Creatine Period (5 days)				Diagnosis and Remarks
			Control gms.	1st gms.	2nd gms.	3rd gms.	
1—N.B.S.	37	Glutamic	0.44	0.73	0.52	0.42	Prog. musc. dystrophy
4—J.B.	34	Glutamic	0.92	1.48	2.11	1.14	Prog. musc. dystrophy
6—G. W.	12	Glycine	0.43	0.96	1.42	0.87	Prog. musc. dystrophy
7—S.W.	10	Glutamic	0.24	0.22	0.10	0.33	pseudo musc. dystrophy
2—L.T.	8	Glutamic	0.29	0.91	0.51	0.51	pseudo musc. dystrophy
3—W.P.R.	10	Glycine	0.28	0.55	0.30	0.29	Prog. musc. dystrophy
5—H.H.	12	Glutamic	0.31	1.02	1.00	1.02	Prog. pseudo musc. dys.
13—C.C.	4	Glycine	0.32	0.57	0.22	0.03	pseudo musc. dystrophy
11—L.B.	43	Glycine	0.17	0.23	0.32	0.15	Myasth. (intraocular paresis, diplopia)
14—E.J.S.	55	Glycine	0.46	0.39	0.39	0.57	Myasthenia of eyelids
8—R.M.B.	11	Glutamic	0.23	0.42	0.19	0.30	Early spino musc. atrop. Progress arrested
9—C.E.C.	28	Glycine	1.63	0.96	0.51	0.63	Strabismus with ciliary weakness
10—J.H.C.	54	Glutamic	0.12	0.36	0.76	0.19	Myasth. right eyelid with diplopia
12—A.S.	31	Glutamic	0.22	0.85	0.00	0.18	Paramyoclonus multiplex
		Average	0.43	0.69	0.60	0.47	
		Per cent increase		60.0	39.5	9.3	

cases as *Table 1* with the addition of one case, No. 15. Of these cases, only five (Nos. 10, 11, 12, 13 and 15) have maintained improvement for a period of 3 to 4 years. Case 10 showed excellent maintained improvement, but died from cerebral hemorrhage.

Table 3 shows a group of 36 cases representing 9 different myopathic conditions in which no objective improvement could be demonstrated, or in which the disease progressed, after a period of several months when treatment was discontinued.

DISCUSSION

The variation in clinical results in various types of cases and in different cases of the same type is indeed quite striking. Of the 51 cases studied, only 5 have shown definite clinical benefit from amino acid therapy alone, or when combined with ephedrin. In these cases, discontinuance of therapy over any period has been accompanied by regression of the beneficial results previously noted. Reinstitution of therapy, however, again resulted in marked benefit. None of the cases has been cured. One case, No. 15, has apparently had a remission as no further progress of the disease has been noted and the clinical improvement has been maintained for 2 years after treatment was discontinued.

Thorough study of the creatine-creatinine metabolism in these cases has thrown light on some of the hitherto complex factors involved. For instance, it was apparent that those cases showing the greatest initial improvement manifested an initial creatinuria which was increased from 50 to 200 per cent upon administration of amino acid and that with continuation of the therapy after several weeks the ceratine excretion fell to the initial level or became minimal. However, as shown in *Table 2*, not all of these continued to show improvement. Some remained stationary after initial improvement and became discouraged and voluntarily discontinued treatment. Usually after several weeks or months retrogression of initial improvement took place and the clinical condition reverted to that of the stage before treatment, or else showed marked progress of the disease.

The results of these studies seem to support the theory that there is an increased creatine retention, as shown by the decreased creatinuria, with subsequent actual increase in muscle creatine after administration of amino acid to such patients.[25 29]

The cases listed in *Table 3*, in whom no objective improvement occurred, showed only a 20 per cent or less increased excretion after the amino acid administration. These cases were those usu-

Table 2

FOLLOW-UP (3-4 YEARS) OF CASES SHOWING INITIAL OBJECTIVE IMPROVEMENT

Case No.	Age	Diagnosis	Remarks
1—N.B.S.	37	Prog. musc. dystrophy	Untraced
4—J.B.	34	Prog. musc. dystrophy	Untraced
6—G.W.	12	Prog. musc. dystrophy	No improvement; therapy stopped
7—S.W.	10	Prog. musc. dystrophy	Improvement temporary; stopped therapy. Bedridden
15—B.G.	10	Prog. musc. dystrophy	Therapy Oct., 1933, to Sept., 1934. Remission
2—L.T.	8	Pseudo musc. dystrophy	Improvement temporary. Stopped therapy. Bedridden
3—W.P.R.	10	Pseudo musc. dystrophy	No change. Stopped therapy. Bedridden
5—H.H.	12	Pseudo musc. dystrophy	Improvement temporary. Stopped therapy. Bedridden
13—C.C.	4	Pseudo musc. dystrophy	Improvement maintained on therapy. Almost normal
11—L.B.	11	Myasthenia gravis	Improvement maintained on therapy. Almost normal
14—E.J.S.	55	Myasthenia gravis	Improvement temporary. Stopped therapy. Same
8—R.M.B.	11	Early spino musc. atrophy	Improvement maintained two years. Untraced
9—C.E.C.	28	Ciliary muscle weakness	Improvement temporary. Stopped therapy. Same
10—J.H.C.	54	Myasthenia and diplopia	Improvement for 1½ years, then death. Cerebral hemorrhage
12—A.S.	12	Paramyoclonus multiplex	Improvement maintained on therapy to date

Table 3

CASES IN WHICH NO OBJECTIVE IMPROVEMENT (OR SUBJECTIVE IMPROVEMENT ONLY) OCCURRED

Case No.	Age	Amino Acid 10-20 gms.	Urine Creatine Period (5 days)				Diagnosis and Remarks
			Control gms.	1st gms.	2nd gms.	3rd gms.	
1	27	Glutamic	0.73	1.67	1.09	0.38	Amyotrophic lateral sclerosis
2	22	Glutamic	0.64	0.93	0.17	0.18	Amyotrophic lateral sclerosis
3	39	Glutamic	0.10	0.09	0.18	0.08	Amyotrophic lateral sclerosis
4	54	Glutamic	0.07	0.07	0.07	0.10	Amyotrophic lateral sclerosis
31	54	Glutamic	0.47	0.39	0.88	0.92	Amyotrophic lateral sclerosis
5	12	Glutamic	0.68	1.63	1.08	0.22	Hypothyroid-pituitary
36	10	Glycine	0.33	0.26	0.74	0.60	Progressive muscular dystrophy
35	8	Glycine	1.14	1.33	1.27	1.23	Progressive muscular dystrophy
9	50	Glutamic	1.19	1.64	0.91	1.39	Pseudo muscular dystrophy
17	12	Glutamic	0.42	0.34	0.30	0.29	Pseudo muscular dystrophy
30	5	Glycine	0.07	0.11	0.10	0.07	Pseudo muscular dystrophy
14	16	Glutamic	1.28	0.68	0.76	0.78	Pseudo muscular dystrophy
6	33	Glutamic	0.09	0.03	0.07	0.16	Multiple sclerosis
18	25	Glycine	0.00	0.12	0.00	0.00	Poliomyelitis
20	7	Glycine	0.15	0.14	0.14	0.12	Poliomyelitis
26	7	Glycine	0.27	0.34	0.21	0.24	Poliomyelitis
27	10	Glycine	0.13	0.32	0.41	0.36	Poliomyelitis
28	7	Glycine	0.20	0.29	0.31	0.30	Poliomyelitis
34	24	Glycine	0.78	0.99	0.81	1.23	Poliomyelitis
13	21	Glutamic	1.26	0.80	0.74	1.20	Muscular atrophy (nerve injury)
33	18	Glycine	0.37	0.58	0.15	0.14	Progressive muscular atrophy
25	8	Glutamic	0.03	0.44	0.24	0.42	Spino muscular atrophy
8	52	Glutamic	0.40	0.94	1.47	1.31	Progressive spino muscular atrophy
11	11	Glycine	0.38	0.33	0.44	0.32	Progressive spino muscular atrophy
7	28	Glycine	0.37	1.49	0.96	0.00	Spino muscular dystrophy
32	5	Glycine	0.34	0.35	0.35	0.45	Spastic paraplegia
19	24	Glycine	0.37	0.27	0.18	0.20	Paresis
21	7	Glycine	0.17	0.37	0.27	0.71	Strabismus
22	7	Glycine	0.74	0.68	0.53	0.31	Strabismus
23	6	Glycine	0.56	0.46	0.28	0.23	Strabismus
24	3	Glycine	0.37	0.23	0.36	0.91	Strabismus
29	24	Glutamic	0.17	0.31	0.25	0.29	Ciliary weakness
10	36	Glutamic	1.43	0.28	0.42	0.69	Friedreich's ataxia
16	38	Glutamic	0.36	0.36	0.28	0.25	"Jake paralysis"
15	21	Glutamic	0.33	0.48	0.53	0.40	Von Recklinghausen's disease
12	55	Glutamic	0.93	1.23	0.16	0.06	Tabes dorsalis
		Average	0.48	0.58	0.47	0.35	
		Per cent increase		21.0	None	None	

ally classified as muscular atrophy secondary to pathologic lesions in the central nervous system or to abolition of function of the lower motor neurone, the so-called second trophic units.

Practically all of our patients noticed remarkable improvement in their appetites; particularly was there a desire to eat protein in the form of meat. There was also a subsequent gain in weight similar to that which occurs in normal individuals after administration of amino acetic acid.[30 31] The increased gastric secretion and possibly gastric contraction would probably account for the increase in appetite. That increased dietary nitrogen, although not affecting pepsin, increased the total amount of gastric juice was shown by Smith and Cowgill.[32] Consequently, the patients noticed distinct improvement in their feeling of well being despite the fact that no objective improvement could be demonstrated.

Dietary protein was not restricted in any of our cases. Reinhold and his co-workers[25] have noted the beneficial effects of combining high protein diets with amino acid therapy. Some observers presenting negative results have restricted protein intake to a minimum.[24]

The stage of the disease when treatment is instituted probably plays an important role in the clinical results obtained. Milhorat[29] has shown that the ability of a muscle to regain its former power depends upon the state of the muscle fibers at the time treatment is instituted. Should the nuclei of the muscle fiber show pyknosis or further degenerative changes, complete degeneration and absorption occurs, despite amino acid therapy. Therefore, when the optimum therapeutic effect of the amino acid is reached, either normal or completely degenerated muscle tissue is seen. Those cases in our series which showed the most striking results were those of children seen early in the disease.

Vitamin deficiency undoubtedly plays a part in the various myopathic diseases. Conwell[33] has recently reported 6 cases of pseudohypertrophic muscular dystrophy in which administration of vitamin D alone produced considerable subjective and objective improvement.

Muscular activity during treatment appears to be quite beneficial to the dystrophic patient, whereas in the presence of inactivity, such as that occasioned by intercurrent illness or operative procedures, the patient becomes rapidly weakened. We have not observed a case where clinical improvement continued after treatment was discontinued. We are of the impression from our results that treatment must be continued for an indefinite period, if not throughout life.

No case, even those seen early in the disease, can be described as "cured." In two instances improvement has been most remarkable and the children appear normal, but on closer examination there is noted persistent muscular weakness. The pseudohypertrophy and increased firmness of the muscle groups appear to remain permanently.

SUMMARY AND CONCLUSIONS

(1) A series of 5 cases of the following 12 different myopathic states has been studied as regards the effect of amino acid therapy over a period of 3½ to 4 years: (a) progressive muscular dystrophy, (b) pseudohypertrophic muscular dystrophy, (c) myasthenia gravis, (d) muscle wasting from disuse, (e) progressive spinal muscular atrophy, (f) subacute and chronic poliomyelitis, (g) multiple sclerosis, (h) amyotrophic lateral sclerosis, (i) muscular paralysis from Jamaica ginger poisoning, (j) muscular paralysis from peripheral nerve section, (k) Friedreich's ataxia, and (l) strabismus.

(2) Those cases classified as primary myopathies of the dystrophic type in which the average creatinuria following amino acid therapy increased from 50 to 200 per cent above that of the control period and later disappeared, showed both initial subjective and objective improvement.

(3) Only two of nine cases of pseudohypertrophic muscular dystrophy which had initial temporary improvement following amino acid therapy maintained this improvement over a 4-year period.

(4) No case has improved to the point of a "cure."

(5) Cases of myasthenia gravis have maintained their improvement over the entire period, but have not been cured.

(6) Cases secondary to brain-cord lesions (subacute and chronic poliomyelitis, multiple sclerosis, amyotrophic lateral sclerosis, muscular paralysis from Jamaica ginger poisoning, muscular paralysis from peripheral nerve section, Friedreich's ataxia and strabismus) which showed the same increase and decrease of creatinuria as those of the preceding group, showed only temporary subjective, but no maintained objective improvement.

(7) The inclusion of amino acetic acid in the diet serves to increase the appetite and body

weight in the majority of underweight individuals and of patients with muscular dystrophy and atrophy.

(8) Amino acid metabolism is probably one of the factors influencing the course of the dystrophic myopathies.

(9) Vitamin deficiency may also play a role in the etiology of these conditions.

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AN ANALYSIS OF FOUR HUNDRED INSTANCES OF CHRONIC BROMIDE INTOXICATION*

By FREDERIC M. HANES, M.D.
and
ANNE YATES, PH.D.
Durham, North Carolina

Chronic bromide intoxication is a widespread and common condition, but it is familiar to relatively few physicians. This is due, in part at least, to the fact that in standard textbooks of internal medicine it is not described. Dermatological texts present the skin lesions of bromidism (which are found in approximately one-fourth of the patients suffering from chronic bromide intoxication) and the psychiatrist[1 2 3] is familiar with toxic psychoses due to bromide poisoning, but the internist frequently fails to consider bromide intoxication in his differential diagnosis. The result is that many puzzling neuropsychiatric cases are incorrectly diagnosed and not a few are wrongfully committed to psychopathic hospitals.[4 5 6]

The records of Duke Hospital show that within the past six and one-half years (January, 1931, to July, 1937) bromide in abnormal amounts has been demonstrated in the blood of more than seven hundred patients, or approxi-

*From the Departments of Medicine and Biochemistry, Duke University School of Medicine, Durham, North Carolina.

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mately 0.9 per cent of the total admissions. In 400 instances bromide in excess of 50 mg. per cent was found, and in this paper we propose to analyze briefly these cases.

We were fortunate in having the interest of the Duke Hospital Clinic, in its very beginning, directed to the widespread occurrence of chronic bromide intoxication by Dr. William A. Perlzweig, Professor of Biochemistry. In 1927, Wuth[6] devised a simple method for the determination of bromide in the blood, and accurately controlled studies of bromide intoxication date from the publication of this paper. The following figures demonstrate the growth of interest in bromide intoxication in the Duke Clinic, showing the distribution by years of 400 instances of chronic bromide intoxication with 50 mg. per cent or more of bromide in the blood: 1931, 10; 1932, 22; 1933, 52; 1934, 70; 1935, 89; 1936, 83; and 1937 (6 months), 74. These figures do not give a complete picture of the incidence of bromide intoxication in this clinic as related to total admissions, though probably including most of the severer cases, 8 of which have been reported by Craven.[7]

The following table (*Table 1*) shows the percentage of blood bromide in 400 patients with chronic bromidism.

In *Table 2* the percentage of replacement of chlorine by bromine in 336 instances of bromidism is shown. (In 64 of 400 cases the replacement value was not determined.)

To obtain an approximate estimation of the incidence of chronic bromidism in general medical patients, blood bromide determinations were made on 500 medical dispensary patients selected at random. Of these 500 patients, 64 (13 per cent) had positive blood bromides, and 29 (5.8 per cent) had 50 mg. per cent or more (*Table 3*).

Bromide determinations are now made in this clinic with almost routine regularity on neuropsychiatric patients. We have found the information obtained comparable in helpfulness to that furnished by the Wassermann reaction. It is an absolutely indispensable aid in the diagnosis of a most puzzling group of cases. For, although experience may sharpen one's suspicions, the clinical manifestations of bromide intoxication are so varied and withal so subtle, simulating every neuropsychiatric condition, that only the positive evidence of bromide in the blood can substantiate the tentative diagnosis. Fortunately, blood bromide determinations are not difficult.[16]* In chronic bromide intoxication bromide is found in the cerebrospinal fluid in quantities only slightly less than those found in the serum.

Bromide intoxication may be mild, severe, or

*A convenient and inexpensive instrument for bromide determinations, the "Wuth Comparator," is manufactured by the LaMotte Chemical Company of Baltimore, Maryland.

Table 1

50-100 mg.%	100-150 mg.%	150-200 mg.%	200-250mg.%	250-300 mg.%	300-350 mg.%	350-400 mg.%
177=44.2%	100=25.0%	59=14.7%	41=10.3%	9=2.3%	8=2.0%	6=1.5%

Table 2

1-10 per cent	10-20 per cent	20-30 per cent	30-40 per cent	40-50 per cent
114=33.9 per cent	132=39.2 per cent	67=19.9 per cent	17=5.0 per cent	6=1.7 per cent

Table 3

Blood bromide +; less than 50 mg. per cent	50-100 mg. per cent	100-150 mg. per cent	150-200 mg. per cent	200-250 mg. per cent
35=7 per cent	17=3.4 per cent	7=1.4 per cent	2=0.4 per cent	3=0.6 per cent

even fatal.[4 8] Several factors influence the accumulation of bromide ions in the blood, where they replace chloride ions. A low intake of sodium chloride favors the retention of bromide ions. Individuals vary greatly in their intake and excretion of sodium chloride; Wuth[6] found that, on hospital diets, patients excreted from 3.5 to 15.8 grams of sodium chloride daily. Since an abundance of chloride ions protects the body against the accumulation of bromide ions, and is capable of displacing the bromide ion of sodium bromide, this factor is of greatest importance in both the etiology and treatment of bromide intoxication. The excretion of sodium bromide is always slow, since the kidney excretes chlorine preferentially over bromine and diuresis does not increase the rate of bromine excretion.[9 10]

Patients react with the widest possible variations to the presence of bromide in the body. Attempts have been made to correlate the amount of bromide in the blood with clinical manifestations, but individual susceptibility and associated disease make it impossible to do this with accuracy. Previous studies, based upon small series of cases, have concerned themselves with the severer manifestations of bromide poisoning, and it is true that greatly disturbed mental states seldom appear until the bromide in the blood reaches 150 mg. per cent or more. Our analysis of clinical manifestations in 400 cases has convinced us, however, that patients having from 50 to 150 mg. per cent of bromide in the blood frequently present definite clinical symptoms of intoxication. It is to these milder intoxications that we wish to draw attention; for unless they are kept in mind they are not only unrecognized, but, worse still, are often treated with bromides, leading to more severe intoxication. Some of the worst poisonings we have observed have occurred in doctors' families, and many of our patients have been sent for study by excellent physicians who had been treating mild symptoms with continuous bromide therapy. Not infrequently such patients had developed mental symptoms justifying the diagnosis of a major psychosis, and were brought for observation before being committed to an institution. Such an error can only be regarded as a great tragedy for the patient, who must bear for the remainder of his life the stigma which the laity attaches to insanity. In most communities patients are committed to psychopathic hospitals by physicians totally untrained in psychiatry. It is of the utmost importance, therefore, that bromide intoxication be considered in every instance of major psychosis, especially toxic - confusional states, coming under the general practitioner's care.

Of 500 consecutive patients admitted to the Colorado Psychopathic Hospital, 7 per cent were found to be suffering solely from chronic bromide intoxication.[4 11] Harding and Harding[5] state that from 3 to 5 per cent of admissions to state hospitals have been found to be due to bromide intoxication, and that in one private neuropsychiatric hospital 4.4 per cent of the total admissions and 23.4 per cent of the toxic-confusional group were due to bromide poisoning.

At our suggestion, three state psychopathic institutions, two in North Carolina and one in South Carolina, are testing for bromides in the blood all patients admitted. The two North Carolina institutions reported that 16 per cent of their recent admissions had 75 mg. per cent or more of blood bromide, and 9.5 per cent had above 100 mg. per cent. Of the patients admitted to the South Carolina State Hospital, 12.4 per cent had blood bromides above 75 mg. per cent, and 7.3 per cent above 100 mg. per cent. The figures quoted in this paper indicate a startlingly high incidence of bromidism, both in general medical and institutional patients.

Craven[7] has given a very clear picture of the clinical manifestations of severe bromide poisoning as observed in this clinic:

> "An individual with one or a variety of medical or surgical complaints has taken bromides during a period of days or weeks. After a variable length of time the patient becomes restless, irritable and emotionally labile, and complains of headache, blurring of vision, interrupted sleep and disordered, usually frightening dreams. As these symptoms endure there are observed weakness, ataxia, slurring and hesitancy of speech, irrelevant conversation, poor appetite and loss of memory, particularly for recent events. Drowsiness and lethargy are soon followed by stupor, and sleep is even more disturbed by disordered dreams. Hallucinations, both visual and auditory, become a prominent feature, and maniacal attacks of excitement are provoked by the fear reaction produced."

Such reactions are seen in severely poisoned patients, familiar enough to the psychiatrist, but the earlier manifestations of bromidism have never been sufficiently emphasized.

Such patients complain of dull morning headache, constipation, indigestion, fatigue, irrita-

bility, sleeplessness, difficulty in concentrating and poor memory. The hands may be slightly tremulous and the gait a little unsteady at times, due to "dizziness." Careful questioning of relatives may reveal that the patient has had brief period of slight disorientation. The picture is one of a mild neurosis, and the usual therapy is bromide sedation. The careful analysis of our own experience shows that these symptoms are very commonly seen in patients whose blood bromides are less than 100 mg. per cent and sodium chloride therapy often results in striking improvement. It is the failure to recognize these milder manifestations of bromide poisoning that leads so frequently to severe intoxication. Bromide alleviates temporarily the symptoms which it produces, and it should be regarded by physicians as a habit-forming drug.

The chief symptoms and signs recorded in the histories of our series of four hundred cases, in order of their frequency, were as follows: (1) headache; (2) irritability; (3) emotional instability; (4) weakness; (5) lethargy; (6) slurring speech; (7) irrelevant speech; (8) delusions; (9) disorientation; (10) hallucinations; (11) loss of memory; (12) cyanosis; (13) vacuous facies; (14) dilated pupils; (15) stupor; (16) blurred vision; (17) fabrication; (18) ataxia; (19) mental confusion; (20) disordered dreams; (21) vertigo; and (22) loss of libido and potentia.

A rash was noted in only one-fourth of the patients. This was usually acne of the face and upper trunk, though now and then papular, or papulopustular in type. The skin manifestations are no index of the severity of the intoxication: of 64 patients with 200 or more mg. per cent of bromide in the blood only 18 (28 per cent) had a rash. It would seem, therefore, that descriptions of chronic bromidism are more urgently needed in textbooks of internal medicine than in treatises on dermatology. Chronic bromide intoxication should be considered in all psychoneurotic patients, that is to say, in the diagnosis of at least one-half the patients who consult physicians.

The highest blood bromide recorded in this series was 428 mg. per cent, with a replacement of chloride of 43.8 per cent. The highest replacement figure was 48 per cent, with a blood bromide of 408 mg. per cent. It is frequently stated that death results from the replacement of 33 per cent of the sodium chloride of the blood by sodium bromide. Our experience does not confirm this, though such a degree of intoxication is unquestionably dangerous and may prove fatal. No death which could be ascribed directly to bromide poisoning occurred in this series of 400 patients.

Bromide intoxication is not infrequently accompanied and aggravated by acetanilid intoxication, since both drugs are very commonly combined in proprietary headache remedies. Sulfhemoglobin was detected in the blood of 65 patients and methemoglobin in the blood of three, indicating an associated acetanilid poisoning. Such patients are often more or less cyanosed.

The sale of bromides is not controlled by legal regulations and an analysis of physicians' prescriptions, made by the American Pharmaceutical Association,[12] revealed that only acetylsalicylic acid is prescribed more frequently. Such prescriptions are readily refilled, leading often to prolonged self-medication by the patient.[8] It is unfortunately true that this danger is not widely appreciated by physicians. Furthermore, it is estimated that more than 200 "patent medicines" containing bromide are on the market, some of which have attained the dignity of household remedies. Headache remedies usually contain bromide; one of the best known of these contains 0.5 grams (7.5 grains) to the minimal dose. We encounter patients not infrequently who take from 5 to 10 such "headache powders" daily.

Treatment is simple and efficacious. Sodium chloride must be given in large amounts. In the beginning we give from 9 to 12 grams daily by mouth. This can be administered in the form of enteric coated pills, or as iced saline solution. Intravenous saline rarely is needed, since it is not desirable to replace the bromide too rapidly. A pleasant method of introducing sodium chloride is in bouillon. One bouillon cube (Swift's, weighing 3 grams) contains approximately 2.4 grams of sodium chloride.

Mason[10] found that human saliva had a greater replacement of chlorine by bromine than blood serum, and inferred that one or more of the human salivary glands preferentially secrets bromide to a marked degree.

Bromide may appear in the gastric juice in concentrations greater than that of the blood,[13] indicating an active secretion of hydrobromic acid by the gastric mucosa. In severe bromide poisoning continuous aspiration of the gastric juice (Wangensteen technic) aids materially in removing the deleterious bromine ions from the body.

Under adequate treatment, even the severest intoxications show improvement within three to seven days.

CONCLUSIONS

(1) Bromide intoxication, more or less severe, is a widespread and prevalent condition.

(2) The clinical picture of mild bromide poisoning is described.

(3) Severe bromide poisoning produces marked mental changes, resulting frequently in the patient's commitment to a psychopathic institution. Approximately 5 per cent of admissions to institutions are due to readily curable bromidism.

(4) Blood bromide determinations, following the method of Wuth, are not difficult, and should be done in all psychoneuroses, and in all cases of intensive or prolonged bromide therapy.

(5) The treatment of bromide poisoning is simple and promptly efficacious.

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GASTRIC ACIDITY AS A MANIFESTATION OF EXTRA-GASTRIC DISEASE*

By FRANK L. APPERLY, M.A., D.Sc., M.D.
Richmond, Virginia

High, low or absent gastric acidity is not a disease in itself as was formerly believed. Gastric acidity in the absence of organic disease is rather the mirror of the blood, or, at least, of certain aspects of blood chemistry, and therefore provides a clue to many deeper metabolic and other changes in the general bodily mechanism.

A knowledge of how the variations in gastric acidity following a standard test-meal are brought about helps us to interpret the conditions present. These variations may be brought about: (a) by local variations in gastro-intestinal muscular or chemical activity, and (b) by certain variations in blood chemistry, dependent on deeper physiological or pathological changes in the body.

(A) LOCAL OR GASTRO-DUODENAL CAUSES

(1) Failure of acid secretion is commonly the result of inflammation or atrophy of the gastric mucosa. A certain proportion of healthy people (about 5 per cent), however, for reasons unknown, also have no acid secretion. In many cases this appears to be an hereditary characteristic, which I have found in four parents and their sons. Similarly high acidity and other gastric "types" are also often hereditary (Apperly and Norris[8]).

(2) The rate of stomach emptying, which, in turn, often depends upon the volume, consistency and osmotic pressure of the food, but since we are assuming the use of a standard test-meal these can be neglected. Normal stomach emptying, then, depends on the neuromuscular activity of the organ, which in turn depends on (among other things) blood pH, and will therefore be considered in Section B. Pathological conditions may, however, raise acidity by causing pyloric obstruction (see 3, below).

(3) Duodenal regurgitation and the alkalinity of the duodenal contents affect the stomach.

(a) Boldyreff[9] first showed that acid placed in a dog's stomach is rapidly re-

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*From the Medical College of Virginia, Richmond, Virginia.

duced, but that if the sources of duodenal alkali are shut off (ligature of pancreatic or bile ducts) the acidity remains high and stomach emptying is delayed.

(b) Apperly[1] next showed variations in gastric acidity among normal students to be due to variations in the ability to neutralize secreted gastric acid rather than to variations in the amount of acid secreted. Thus people who normally have hyperchlorhydria have difficulty in neutralizing or reducing 25 c. c. of .4 per cent HCl artificially placed in their stomachs, whereas those who normally have hypochlorhydria readily reduce the introduced acid (*Figs. 1* and *2*).

(c) Apperly and Cameron[5] similarly showed that in pancreatic disease with deficiency of alkali production there is a rising acidity with the test-meal and a delayed neutralization when acid is artificially introduced into the stomach (*Fig. 3*).

(d) The same phenomena are shown in the pyloric spasms of duodenal ulcer (Elman[10]) and of appendical disease (Levy[11]).

(e) Conversely the rapid emptying and free duodenal regurgitation after gastroenterostomy lead to a rapid reduction of acidity (Apperly[2]).

(4) In 1926, I[3] showed that when acid of 0.08 to 0.10 N was introduced into the stomach in man secretion of acid was depressed or inhibited. Recently Wilhelmj and others,[13] by more exact methods, showed the same in dogs and further, that acid entering the duodenum has a similar effect; in brief, that acidity is automatically regulated even in the absence of

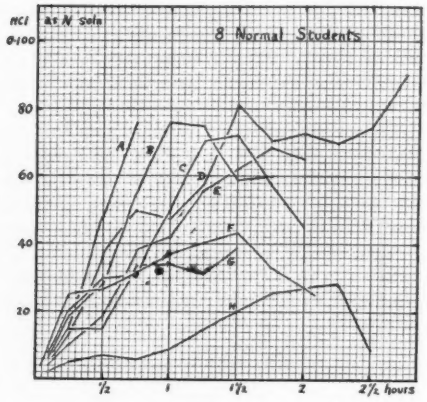

Fig. 1

Fractional test-meal curves (gruel meal) in eight normal students (for comparison with Fig. 2).

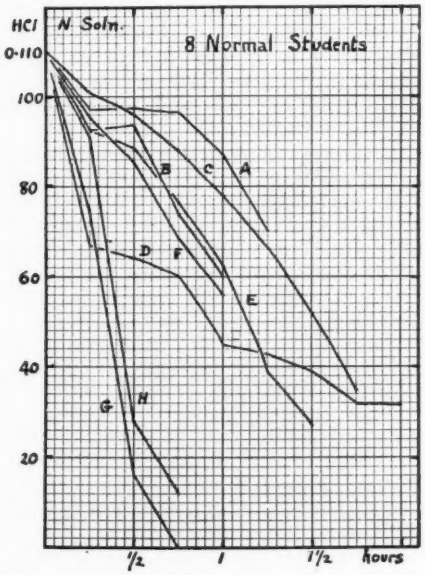

Fig. 2

Showing the fall in acidity in eight normal students (same as those in Fig. 1) when 250 c. c. of 0.110 normal hydrochloric acid is substituted for the gruel meal.

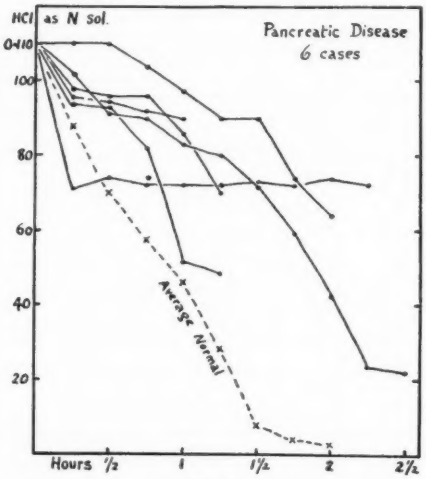

Fig. 3

Showing delayed acid neutralization or reduction in six cases of known pancreatic disease. (Normal average curve also shown.)

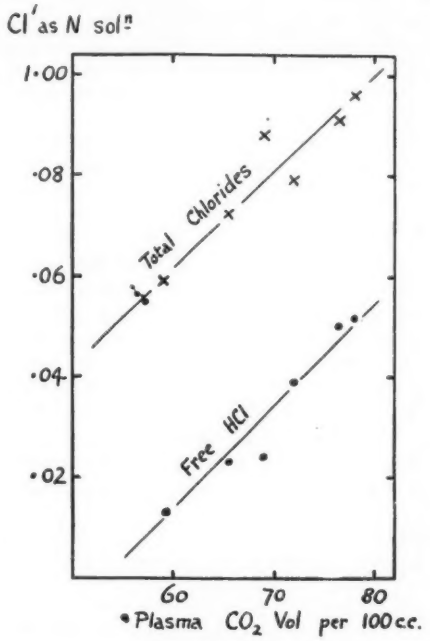

Fig. 4

Showing the relationship of (a) total chloride, and free hydrochloric acid of gastric contents one hour after the commencement of a test-meal to (b) the carbon dioxide combining capacity of the fasting blood plasma in one individual under various conditions of experimental acidosis, alkalosis, and so on.

duodenal regurgitation. Such a cessation of acid secretion would therefore be expected to result in a level acidity curve. However, the fact that in most cases acidity drops to lower levels towards the end of a test-meal, together with the evidence summarized in Section 3, above, would appear to show that duodenal regurgitation is of greater importance in regulating the concentration of acid in the stomach.

(B) CHANGES IN BLOOD CHEMISTRY, ESPECIALLY HYDROGEN-ION AND CARBON DIOXIDE CONTENT

(1) Gastric acidity varies with the sodium bicarbonate content of the blood plasma of the fasting healthy subject (Apperly and Crabtree,[7] *Fig. 4*).

In disease the same law holds. Thus, as summarized in *Table A*, any condition which is associated with diminished plasma CO_2 or $NaHCO_3$ results in lower gastric acidity, for example: high external temperature, tropics, fevers, high altitudes, diabetes, chronic nephritis, severe exercise, pregnancy, menstruation, severe hemorrhage and poor physical fitness.

On the other hand, any condition that raises plasma $NaHCO_3$ is found to be associated with a higher gastric acidity, for example: ingestion of alkaline salts, Sippy's diet, insulin in normal or diabetic subjects, sleep and the experimental breathing of carbon dioxide. As shown in *Table A* (c), we also find that different types of body build are associated with corresponding alterations in gastric function. Thus people with relatively large lungs (that is, large pulmonary vital capacity per unit of body weight or of body surface) usually tall, thin people, are found to have a higher acidity and rather more slowly emptying stomachs, together with a raised alveolar carbon dioxide pressure (Main[12]). It would therefore appear that these individuals have a large oxygen absorbing surface, are well aerated, and breathe more slowly, with consequent retention of CO_2 and a higher blood $NaHCO_3$. In my experience the majority of Grade A students fall into this group with high acidity. On the other hand, people of poor physical fitness, the common hospital out-patient type, have an unusually high proportion with low acidity.

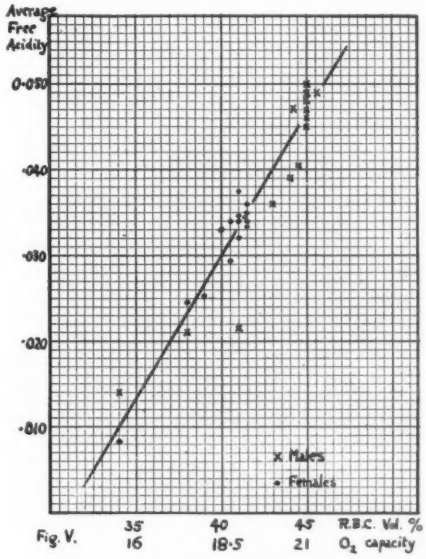

Fig. 5

Showing the relationship of (a) the average normal gastric acidity of different age and sex groups (taken from 3,746 cases by Vanzant, Alvarez, *et al.*) to (b) the average normal hemoglobin of different age and sex groups (from Peters and Van Slyke).

(a) PRIMARY CO_2 DEFICIT

—	Plasma CO_2	Blood pH.	Gastric Acidity	Gastric Motility
	Dim.	Inc.	Dim.	Inc.
Hyperpnoea	4, 5, 6	4, 5, 6	3, 13	....
Hot room	7	7	14	....
Hot baths	8, 9, 10	10	15	15
Tropics	11, 12	12	16	....
Fevers	9, 22	9	20, 21	....
Altitudes	50, 51, 52	50	71, 72	....
Encephalitis	73, 74	73	....	....
X radiation	23, 24, 25	23, 24, 25	....	26
Some cardiac failures without pulm. comp.	75, 76	....	....	....

(b) PRIMARY ALKALI DEFICIT

—	Dim.	Dim.	Dim.	Dim.
Ingestion of amm. chloride or HCl	27,28,77,2	28, 77	2, 3	2
Chronic nephritis	41 et al.	41	39, 40	....
Diabetes	78, 25	78, 25	Tk.	....
Severe exercise	35, 36, 74	35, 74	34	34
Menstruation	38	....	83	....
Pregnancy	31, 32, 33	No pH changes reported.	29, 30	....
Anoxemia chronic	53, 4	53, 4, 81	54, 72	54, 72
Hemorrhage severe	48, 49	48, 82	Fig. 2	91
Poor physical fitness	38, 64, 15	....	37	15
Starvation	79	79	46	....
Infantile diarrhea	80	80	....	....
Some cardiac failures near death	75	75	....	....

Tk.=Textbook statement.

(c) PRIMARY CO_2 EXCESS*

—	Inc.	Dim.	Inc.	Dim.
Breathing CO_2	57	84, 85	2, 3, 61	2
Sleep	63	—	62	62
Large—† V.C. W. or — V.C. S.	86‡	87	15, 66	67, 15
Emphysema	58, 59, 60	59	....	....
Asthmatic attacks	38, 72	....	....	....
Certain cardiac failures with CO_2 retention	75, 88	75, 88	....	....

*This group is often complicated by anoxemia, hence may overlap Group (b). †Vital capacity divided by body weight. ‡Alveolar CO_2.

(d) PRIMARY ALKALI EXCESS

—	Inc.	Inc.	Inc.	Inc.
Ingestion of alkaline salts	57, 68,69,2	57, 69	2,3,89,90	2
Sippy diet	24, 25	24, 25	2, 70	....
Insulin following diabetic acidosis	....	....	42, 43, 44	45

Dim.=diminished. Inc.=increased.
Pulm. comp.=pulmonary complications.

Table A further shows the variations in blood pH and gastric motility under the various conditions listed. It will be noted that whereas gastric acidity varies with the plasma CO_2 or $NaHCO_3$, on the other hand gastric motility varies with blood pH. That is, conditions in which blood alkalinity is increased are associated with more rapidly emptying stomachs, while some delay occurs in conditions associated with a trend towards a less alkaline condition.

(2) Certain anemias, especially those following acute and chronic hemorrhages, are associated with a falling gastric acidity and, if severe, with achlorhydria. As the anemia improves, acidity rises. As the red cell content rises beyond normal, however (polycythemia) acidity again falls (*Fig. 5*, Apperly and Cary[6]).

It will thus be seen that achlorhydria is associated with three types of anemia, namely: pernicious anemia, the achlorhydric anemia of Witts, and with what we have called anemic achlorhydria.

SUMMARY

(1) High, lower or even an absence of gastric acidity is now known to be perfectly normal in certain human types, and is not, as was formerly taught, a disease in itself or the cause of symptoms.

(2) Gastric acidity variations can be brought about by: (a) local variations in gastro-duodenal muscular or chemical activity, and therefore are often typical of various types of dysfunction, and (b) by certain variations in the chemical constitution of the blood, which in turn is dependent on other bodily changes.

(3) A knowledge of the changes in gastric acidity and the processes by which they are brought about may provide valuable clues to certain metabolic changes in the body and their causes. The stomach, in short, is the mirror of certain general bodily functions.

(4) Achlorhydria is associated with three classes of anemia, namely: pernicious anemia, the achlorhydric anemia of Witts, and anemic achlorhydria (Apperly and Cary).

Table A. — Showing the relation of gastric acidity and emptying time to plasma $NaHCO_3$ and pH.

Acidity varies with plasma $NaHCO_3$ irrespective of pH.

Motility varies with blood pH irrespective of plasma $NaHCO_3$.

(The figures denote references to authors in a paper by Apperly[4]).

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DISCUSSION (*Abstract*)

Dr. Julian M. Ruffin, Durham, N. C.—The regurgitation of the duodenal contents as a regulating mechanism of gastric acidity has long been recognized. While there are many other factors, this regurgitation is probably one of the most important in lowering gastric acidity.

Dr. Apperly says that the carbon dioxide content of the blood plasma is likewise a controlling factor, and that gastric acidity can be varied at will by raising or lowering the blood carbon dioxide. While some investigators have confirmed this finding, others have failed to do so: and personally, I am rather inclined to doubt that the blood carbon dioxide is an important factor in the determination of gastric acidity.

The role that is played by emotional or nervous factors is frequently overlooked. Beaumont was the first to note that anger or fear would inhibit or even entirely suppress gastric secretion. This will necessarily lower gastric acidity and is probably responsible for the wide range of values that is frequently noted in any one individual. Gastric motility is likewise markedly influenced by nervous stimuli, and motility in turn directly affects gastric acidity.

From my own experience, I do not feel that the acid values obtained from a single analysis done in the conventional manner, either with the test meal or after histamine stimulation, have any great significance. It is common knowledge that in health, as well as in disease, the patient may have acid values ranging from zero to one hundred or more. A patient with a duodenal ulcer may have no free acid and patients with carcinoma of the stomach may show normal acidity.

While I do not advocate abandoning the procedure, as it has definite therapeutic value, I feel it unwarranted, except in cases of achlorhydria, to attach any significance to the amount of free hydrochloric acid reported.

Dr. Apperly (closing).—In reply to Dr. Ruffin's questions concerning the high acidity found in many patients with nervous dyspepsia, I have no definite answer, but in many cases I have noticed that there is a hypertonicity and hypermotility. Under these circumstances duodenal regurgitation would be reduced to a minimum, or indeed might be absent. The acidity of the gastric contents would therefore remain high just as it is in cases of pyloric obstruction. I have considerable evidence that this is the reason for the high acidity in duodenal ulcer even when there is no obstruction.

ETHYL ESTERS OF CHAULMOOGRA OIL THERAPY IN THE TREATMENT OF MYCOSIS FUNGOIDES*

By SIDNEY J. WILSON, M.D.
Fort Worth, Texas

My first contact with mycosis fungoides, in actual treatment, was in 1914, when an elderly patient came under my care. He had been afflicted for some ten years and was then in the terminal stage. From an insidious beginning on his lower legs, the infection had grown progressively worse until every portion of his body was affected, with the exception of the palms of his hands and the soles of his feet. X-ray therapy had no influence on the itching, but did cause disappearance of individual tumors and ulcers. However, similar lesions appeared in new areas rapidly, and eight months later the patient died. This case is mentioned merely to demonstrate the comparative ineffectiveness of recognized treatment in mycosis fungoides.

After reading of the experiences and treatments instituted by Lumholdt,† it was my belief that a mixture of the ethyl esters of the various unsaturated acids of chaulmoogra oil might prove an effective therapy in the treatment of this disease. When, a few months later, another patient, aged 68, came under my care and his affliction was diagnosed as mycosis fungoides, opportunity arose to try this therapy. X-ray had been used, but the patient grew steadily worse. When he was subjected to the treatment involving the use of ethyl esters of chaulmoogra oil and x-ray therapy discontinued, his condition improved noticeably.

Case 1.—P. B., aged 68, white, construction foreman of a railroad, consulted me March 28, 1935, complaining of a skin eruption that he first noticed in January, 1933.

His family history was negative. He had been married for 42 years, had two grown sons who were healthy, and he had always enjoyed excellent health. His wife was living and well. The onset of his skin irritation

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†Lumholdt: Anti-Leprol in the Treatment of Mycosis Fungoides. J.A.M.A. (April) 1935.

began with an itching sensation around his ankles, which he attributed to contact with creosoted lumber. Avoidance of this contact and the application of various local medications failed to give relief. He consulted a physician, who treated him for "eczema." The eruption continued to spread and the itching had become so severe during the preceding year that he had to discontinue his work. In the last six months he had lost about 25 pounds.

Although the weather was mild, the patient was wearing an overcoat and complained of being cold. He was somewhat emaciated and presented a distressed facial expression. The blood count was within normal limits; the Wassermann test was negative. The cervical lymph nodes were palpable. The skin presented a multiformity of lesions. There were numerous excoriations and areas denuded of epithelium from scratching. The abdomen showed numerous scaly lesions interspersed with apparently normal skin. The skin of the forehead was thickened and covered with scales. The surface of the shoulders, lumbar regions and buttocks presented the general appearance of an extreme seborrheic dermatitis with large irregular shaped infiltrated areas. The lower extremities presented numerous eczematoid patches.

One-fourth skin unit applications of x-ray were instituted, successive areas being treated until the entire surface of the body was covered. There was not the slightest cessation of the intense itching. Temporary relief from the pruritic attacks was had following a warm starch bath and going to bed in a super-heated room.

Two months after the initial visit to my office the patient complained of a painful nodule in the left lower quadrant of the abdomen. Examination disclosed three plum-colored lesions, the largest being approximately the size of an English walnut. A filtered x-ray application was given to this area and the patient was sent to St. Joseph's Hospital. Morphine was given for rest and for relief of the intense itching. Three days after being admitted to the hospital the first gluteal injection of 2 c. c. of ethyl chaulmoograte was given, on the third day 3 c. c., and on the sixth day 3 c. c. At this time morphine was discontinued and the intervals between the gluteal injections were lengthened to five days. There was a complete cessation of the itching after the third gluteal injection. He was discharged from the hospital on the twenty-first day. His condition continued to improve, but, at irregular intervals, he had mild pruritic attacks of short duration. At the end of six months there was such marked improvement that the injections were discontinued. At this period the skin on the back and lumbar regions still showed areas of desquamation, but the board-like infiltration had disappeared and he had regained his weight. After a rest of two months, without medication, there was an acute exacerbation resembling an urticarial attack. The injections were resumed, 3 c. c. given at six-day intervals. This was continued until three weeks before his death in July, 1936. The family physician stated that heart disease was the cause of death.

This patient was given treatment over a period of fourteen months, with a rest period of two months. From the time he left the hospital until three weeks before his death, his physical condition was good. He took daily walks about his neighborhood and, at appointed times, came to my office for treatment.

Case 2.—S. T. M., aged 65, white, a sheetmetal worker, consulted me November 4, 1935, complaining of a disorder of the skin that had been bothering him four or five years.

He had had rheumatism for eight years, but worked hard at his trade. The onset of his trouble was on his ankles and the calves of his legs. Four or five years after the onset the skin irritation had spread until most of the surface of the body was involved.

This patient, like *Case 1,* complained of being cold. His normal weight was 140 pounds, but at examination he weighed 130 pounds. He had had several Wassermann examinations of the blood, all negative. The cell count and blood pressure was within normal limits. The skin on the forehead presented a corrugated appearance, covered with small bran-like scales. His cheeks showed numerous scratch marks, and he had plaque-like lesions on his shoulders and buttocks. Most of the surface was dull red in color, but many small infiltrations had a yellowish cast. There were two groups of tumors; one located in the right inguinal region, the other in the right popliteal space. The central lesions were deep purple in color and extremely painful to touch.

Filtered x-ray applications were given to the tumor areas and the injections of ethyl chaulmoograte were instituted, 3 c. c. being the initial dose. As the patient lived some three hundred miles away, he was advised to continue this treatment under the care of his family physician, Dr. Joel Shelton. Dr. Shelton gave him two 3 c. c. gluteal injections each week for six months, then increased the dosage to one every third day and continued without interruption for a year. During the first six months there was very little, if any, improvement in the skin condition. Several small, deep-seated tumor masses appeared on different parts of the body. These responded to x-ray therapy.

In June, 1936, the skin lesions began to disappear, this being about eight months after the institution of the ethyl chaulmoograte therapy. The skin remained almost normal for a period of two months, when there was an acute reaction. This reaction subsided on all areas except the abdomen and chest, which remained the color of raw beef. This remaining erythema may have been due to heat, as the patient remained constantly before a hot stove.

In February, 1937, fourteen months after the patient first consulted me, he had an apoplectic stroke with loss of speech for three days. Despite the fact that he was placed in a room without heat, he did not complain of being cold. The itching that had been constant for years subsided. The gluteal injections were discontinued after the above mentioned attack. Except for pain in the left foot, he was comfortable although confined to bed. His skin remained clear until he died four months later. The cause of death was mycosis fungoides, embolus at the base of the brain.

Case 3.—C. H. R., aged 39, a white business man, consulted me August 27, 1935, complaining of an itching eruption on his lower legs that had annoyed him for five years.

The family history was negative. He had been married fourteen years, had two healthy children, and his

wife was living and well. Several x-ray applications had been given without improvement in his condition.

This patient was an unusual physical specimen, being 6 feet 3 inches tall and weighing 270 pounds. A complete physical examination did not disclose any abnormality except the skin irritation on his lower extremities. Though confined to the areas between the knees and the ankles, the general skin picture of these parts presented a multiplicity of lesions. The irritation around the ankles resembled an eczema rubrum. On the shins were lesions resembling psoriasis. There were also small, irregular shaped areas of normal skin. The skin on the calf of the right leg was covered by infiltrated plaques. The central ones showed rounded nodules firm to the touch. The central lesions were plum-colored. The peripheral lesions had a yellowish cast. The calf of the left leg showed lesions similar to the right, but the area involved was not so large.

Ethyl chaulmoograte, 2 c. c., was given and the patient advised to have his family physician continue the same dosage at four-day intervals. He was requested to make a weekly report of his progress, which he failed to do. I next saw him on December 5, 1935, approximately three months later. The skin covering the ankles and shins was normal. The skin on the calves of the legs was thin and pliable and showed irregular areas of brownish pigmentation. The patient stated that "after he had had the fifth gluteal injection there was a complete cessation of the itching and that within a period of two months the eruption had disappeared." He was advised to continue treatment for sixty days longer.

I saw this patient in March, 1936, and in January, 1937. He was enjoying excellent health and there was no evidence of a recurrence.

Case 4.—S. D. T., aged 39, a white farmer, consulted me March 23, 1937, complaining of a disorder of the skin that began on his lower extremities in the summer of 1929.

He had had measles and whooping cough during childhood and otherwise had always enjoyed good health until his present trouble. His father was living, aged 91. The patient had consulted several physicians since the beginning of his trouble. He was told that he was allergic to several foods and plants; was advised to adhere to a rigid diet and to move to the sea coast. In 1930, he moved to the Rio Grande Valley, about fifty miles from the Gulf of Mexico. There being no improvement in his condition, he consulted a physician, who gave him intravenous injections, the character of which was unknown to him. His skin condition grew much worse. The irritation at this time had spread over most of his body. He was confined to bed for a period of several months. During his confinement his skin was covered with scales and the itching was intensified. During the six years he lived in this section he was unable to perform any sort of manual labor. In December, 1936, he moved back to his home in north Texas.

This patient, like *Case 1,* complained of being cold. When I first saw him he was wearing an overcoat, two suits of clothes, and heavy underwear. He had lost about 35 pounds during the five-year period. His normal weight had been about 170. The extensor and flexor surfaces of his forearms showed a multiplicity of lesions. Those around the wrists had become confluent. They were dull yellow in color and were only slightly infiltrated. The skin around the elbows showed numerous circumscribed, ham-colored infiltrations that were irregular in outline. The entire surface was covered with scales. The buttocks and lower limbs presented numerous lesions similar to the above. The calves of the legs showed a conglomerate group of infiltrated nodular lesions. There were numerous scratch marks over the entire skin surface.

The patient was given 2 c. c. of ethyl chaulmoograte and advised to eat a balanced diet. This dosage was continued at five-day intervals for one month. After the third treatment there was a decided improvement in the patient's general condition. He discarded excess clothing. He was having only one or two mild pruritic attacks weekly, and he was able to do light work on the farm. This dosage was increased to 3 c. c. one month after beginning treatment, but, on account of severe skin reaction and intense itching following the larger dose, the treatment was discontinued for five weeks. During this period the patient was doing manual labor on the farm. From June 1 to November 15, 1937, the patient has not had more than twenty gluteal injections at irregular intervals. He seems to make better progress on a smaller dosage, 1 to 1.5 c. c. The only pruritic attacks that he has had since June 1 were caused by the increased dosage. This has happened twice when the 3 c. c. injections were given as tests.

This patient now weighs 160 pounds, having gained 25 pounds. Except for the skin on the calves of his legs and his lower abdomen, he is free from skin manifestations The calves of his legs show hyperpigmented areas with mild infiltration. On the lower abdomen there are several circular, brownish colored bands surrounding apparently normal skin. This patient does not appear regularly for observation and treatment.

SUMMARY

(1) Four patients, with mycosis fungoides, were treated with ethyl chaulmoograte, a preparation obtained from chaulmoogra oil.

(2) There were no sequelae nor the slightest discomfort to the patients following the injection of this preparation.

(3) Relief from the accompanying pruritus was obtained in three cases soon after beginning treatment, and in the other one four months before death.

(4) Dosage suitable for each patient must be determined by clinical tests.

(5) X-ray therapy is of decided value in the tumor stage, but does not influence the accompanying pruritus.

As only four cases were treated by this method, it is impossible to reach any definite conclusions regarding the effectiveness of the use of the ethyl

esters of chaulmoogra oil. They are reported with the hope that usage by others may prove definitely whether a step forward has been made in the treatment of this disease.

DISCUSSION (*Abstract*)

Dr. James Grant Thompson, Jackson, Miss.—The first cases treated with chaulmoogra oil have already been mentioned by Dr. Wilson. Dr. Svend Lumholdt, Copenhagan, reported a second series of cases in *Acta Dermatologie-venereol,* September 1936, in which he says, "In mycosis fungoides, all six patients treated showed considerable improvement, and in several there was complete disappearance of the nodules." The oil used by Dr. Lumholdt was hydnocarpus oil, chaulmoogra oil, and the ethyl esters of various unsaturated oils. He gave the oil intramuscularly in 1 to 3 c. c. injections with one per cent benzocaine. He also gave it intravenously, twenty per cent emulsion in ten per cent alcohol. This was sometimes followed by quite a bit of coughing and other untoward symptoms. The oil can be given by mouth in gelatin perles. Dr. Fred Wise told me that he treated two cases at the New York Post Graduate Skin and Cancer Unit and saw no improvement.

In all, we know of twelve patients who have been treated, nine of whom were benefited. The prognosis of mycosis fungoides being what it is, any method of treatment that offers any relief whatsoever is worth trying. It is quite probable that more mycosis fungoides would be recognized earlier if biopsies were done upon all cases where there is a doubt as to the diagnosis.

Dr. Rowland W. Hall and I have a case of mycosis fungoides under observation that we hope to treat with chaulmoogra oil.

Dr. Frank W. Riggs, Montgomery, Ala.—The multiplicity of remedies that have been and are still used in this condition is evidence of their inefficiency. The best of these, which appear to be radiation and fever therapy, offer only temporary relief. Fever therapy was suggested by the occasional spectacular improvement following an acute infection with high temperature. The hyperpyrexia from malaria inoculation appears to be more beneficial than mechanically induced fever.

The use of chaulmoogra oil was first reported by Lumholdt, who claimed favorable results in four cases treated; O'Leary, on the other hand, stated that his results, using the same methods, were disappointing.

Before we can hope for any real success in treatment, we must clarify this tangled mass of facts and opinions which are now called mycosis fungoides.

Dr. Wilson (closing)—Biopsy reports are routine in my office where it is possible to assist in a diagnosis. In the premycotic stages of mycosis fungoides reports from three laboratories have not been of assistance as all of them reported "inflammatory tissue." I think the pathologist should possess special knowledge to be of assistance in the examination of tissue taken in the first and second stages of this disease.

When tumors and ulcers develop, a clinical diagnosis may be readily confirmed by biopsy.

MYCOTIC INFECTIONS IN OTOLARYNGOLOGY*

By WILLIAM D. GILL, M.D.
San Antonio, Texas

It is interesting to note in reviewing the history of the development of bacteriology that discoveries in the realm of mycology antedated those in the field of the fission fungi or bacteria by an appreciable number of years. The veil of mystery surrounding microscopic forms of vegetable life was lifted for the first time, and only partially then, to the investigative eyes of Hooke who, in 1677, discovered certain forms of microscopic life infecting rose leaves and found that the yellow spots which he examined with his crude magnifying device consisted of filamentous fungi. It was not until 1722 that the Dutch scientist Van Leeuwenhoek made public his observations on certain microorganisms which he designated as "wretched beasties," in which he described motion as an attribute, and for the first time in history organisms were revealed in the class which we now designate as bacteria. Thus it is recorded that an interval of forty-five years separated the observations of these two men of science. The investigative work of Langenbeck,[1] in 1839, revealed the cause of thrush in mankind to be a parasitic fungus which attacked the mucous membrane of the oropharynx. This was the first fungous disease affecting mankind in which the causative organism was definitely identified. It was further studied by Charles Robin,[2] who in 1843 named the microorganism *Oidium albicans*. In 1839 Schoenlein discovered the cause of favus to be a fungus. In 1844 the fungus causing tinea circinata was announced by Gruby and Eichelstedt, and in 1846 they found the etiological factor in pityriasis versicolor to be a fungus.

With the discoveries of Robert Koch and Pasteur in the realm of bacteriology, medical men turned their efforts to this field of investigation, and for many years medical mycology received scant attention. A revival of interest in medical mycology occurred in the latter part of the Nineteenth Century, and with improvement in methods of investigation it assumed an increasing importance and many of the fungi which had previously been regarded as harmless but

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troublesome invaders of cultures were linked with diseases in mankind. The name of Castellani is outstanding in medical mycology because of the enormous amount of investigative effort which he has spent in this field and the fund of knowledge which medical men have acquired concerning fungous diseases is largely the result of his labors. Certain taxonomic difficulties have been overcome, but some of them persist, and in the classification of certain of the fungi there remains considerable difference of opinion.

The widespread distribution of fungi in nature is in a large measure responsible for the occurrence of mycotic infections in which mankind is the victim, though many of these diseases are also scourges to lower forms of life. Tinea infections occur in the feline and bovine groups and coccidiosis occurs in fowls.

The incidence of mycotic infections is much higher than is generally supposed and the diseases coming within the province of otolaryngology attributable to fungi occur with sufficient frequency to merit serious consideration.

The surfaces of the oral, pharyngeal and nasal mucous membranes, as well as those of the deeper structures such as the larynx, trachea and bronchi, may be contaminated with harmless fungi or pathogenic varieties may attack any or all of these structures and produce serious lesions in them, though their ability to do so varies somewhat and is probably due to different degrees of pathogenicity in the organisms encountered, but also in a measure to the host's resistance to infection with them. Many of the fungi which are ordinarily either harmless parasites or saprophytes may become facultatively pathogenic.

Some of the fungi which may be mentioned as the causes of lesions coming within the domain of otolaryngology are the Actinomyces, the Blastomyces with their subdivisions, the Torulae, Oidia, Monilia, and Saccharomyces. The Coccidioides are often considered in the same heading as the Blastomyces, but differ culturally and morphologically from the other members of the group. The Aspergilli, Penicilia, Sporotrichi, Leptothrices and the Mucoraceae are also of importance to the otolaryngologist.

Extension of fungus infections into the larynx and bronchopulmonary tree and lung tissue is not uncommon, and many observers who have written on this subject emphasize their belief that mycotic infections in these areas are more frequent than is generally supposed. Failure to recognize them is generally attributable to improper methods of obtaining material for cultural study, improper or inadequate cultural methods, or failure to make a critical differential study of the pathologic picture presented by the patient. Looper[3] says that mycotic infections are sufficiently frequent to be considered in all undiagnosed pulmonary infections, and that in the final analysis diagnosis resolves itself into a bronchoscopic problem; for by this means alone are secretions to be obtained for cultural study without contamination with other organisms present in the upper respiratory tract. Mycotic pulmonary diseases run a clinical course greatly similar to that of tuberculosis. There is a slightly greater tendency to hemorrhage, but nothing else, even in the x-ray pictures, which is definitely diagnostic, and diagnosis rests finally with the cultural studies and the absence of tubercle bacilli in the sputum. Looper has recently reported eleven assorted cases of mycotic infection of the lungs, in all of which the disease could have been easily confounded with pulmonary tuberculosis, but which were properly diagnosed by bronchoscopic examination and cultural studies. He strongly emphasized the advisability that tuberculosis sanatoria have an associated bronchoscopic clinic; for the treatment of mycotic infections and of pulmonary tuberculosis is diametrically opposed, one benefiting from the use of iodides, which in the other condition would prove disastrous.

Other writers[4-10] have reported mycotic infections in the pulmonary system due to Monilia, Aspergilli, and the various yeasts, and their observations support the belief that such diseases are by no means medical curiosities, but that they are often overlooked or undiagnosed.

Blastomycosis includes infections with four types of organisms which are more or less closely related and are sometimes called "wild yeasts."

Blastomycotic dermatitis may occur in the areas surrounding the external ear or about the mouth or nostrils.

Laryngeal blastomycosis has been described by Jackson,[11] New,[12] Clerf and Bucher,[13] Downing,[14] Dennis,[15] and others.[16 17] New[18] and New and Childrey[19] have reported involvement of the tongue with blastomycosis. Alvarez[20] has reported a filamentous lesion of the dorsum of the tongue due to a yeast-like organism which was classified as a chromogenic (red producing) Torula.

In the mucous membranes of the oropharynx Torulae cause lesions of an indurative character,

with only slight accompanying inflammatory symptoms, but with pain out of proportion to the extent and degree of the local lesion. Subsequent softening and breaking down of the center of the lesion gives rise to an ulcer covered with yellowish-white exudate which, when wiped away, leaves a granular base. There is a variation in the appearance of the local lesions which probably depends upon the density of the tissue in which they occur. The responsible organism can be recovered from the wound exudate and may also be found in curettings and in the tissue surrounding the ulcer.

In certain lesions suspected of being mycotic in nature, biopsy is at times necessary to establish diagnosis. The method of Weidemann[21] is particularly applicable to the diagnosis of Torula infection in tissue specimens.

Torulae have a marked predilection for the nervous system which they invade and in which they produce a low grade, highly fatal type of meningo-encephalitis. It is generally believed that a local lesion, usually in the upper respiratory tract, represents the atrium through which the Torulae gain access to the nervous system and that the prompt eradication of the primary focus will in most instances prevent the more serious type of involvement. Lloyd Jones,[22 23] in an analysis of cases of Torula meningo-encephalitis reported prior to 1927, found that local lesions in the upper respiratory tract antedated the central nervous system involvement in a high percentage of patients.

Oidia cause a type of infection which is fairly common in infants and is the oldest mycotic infection of which we have knowledge. It is the thrush of older writers and is oftentimes referred to as aphthous stomatitis. Oidia are considered as a species of the Monilia genus by many authorities on medical mycology.

Saccharomyces are often found in surface cultures taken from the nose and throat. They may on rare occasions assume a pathogenic role and produce lesions similar to the Oidia.

Coccidioides usually gain access to the body through the respiratory tract. A recurrent rhinitis similar to a cold in the head, and not yielding to the usual methods of treatment, often marks the onset of coccidiosis. Systemic coccidiosis involves the viscera, bones and joints, and is a highly fatal, fulminating type of disease. Coccidia may cause ulcerations of a granulomatous character involving the mucocutaneous junctures about the mouth and nose and in such instances it may be relatively benign in its course. One should not fall into the error of considering it a condition strictly limited to one geographic zone, though it is more prevalent in some areas than others. It is probably more widespread than is generally supposed.

Actinomycosis may attack the tongue or other mucous surfaces in the oropharynx. Its site of origin is characterized by a deep-seated nodule, which increases in size and eventually ruptures and discharges granules which are characteristic of ray fungus infection and in which the responsible organism is found. Extension takes place peripherally and is accompanied by the occurrence of thick, brawny induration.

Leptothrix infection is encountered fairly often in the tonsillar region. In this type of infection white, warty masses are encountered growing from the tonsil crypts. Leptothrices may be encountered in throat cultures without a definite pathological process being present. Their pathogenicity is of a low order and the infection which they produce, while puzzling at times, is not regarded as dangerous. The lesions caused by Leptothrices are difficult to clear up by either local applications or constitutional treatment, and are best eliminated surgically. They have no apparent influence on the healing process afterward, or if there is an effect, it is so slight that it is not of any practical importance.

Sporotrichosis may be due to infection with one of several species of Sporotrichum. It produces a granulomatous type of lesion which may be confined to the skin and subcutaneous tissues, or it may become systemic and cause lesions in the viscera, bones, or central nervous system. Lesions of the oral, lingual, pharyngeal, laryngeal and conjunctival tissues due to this organism have been described.[24-28] Cervical adenopathy may occur in the lymphangitic forms and may cause pulmonary involvement which resembles tuberculosis. I have had a patient under observation who had pulmonary invasion with this fungus and involvement of the left kidney and the skin of the lumbar region and buttocks in indolent abscesses.

Some individuals apparently have an immunity to the usual mycotic infections, while others are especially vulnerable to them.

Fungi may invade the nasal accessory sinuses, a recent report on this condition having been made by Stevenson.[29] Iglauer[30] reported an instance of pneumocele of the frontal sinus which was thought to be secondary to blastomycotic infection.

Two instances of invasion of the nasal acces-

sory sinuses by Torulae have occurred in my practice. In one patient the ethmoidal labyrinth on the left side was invaded and in the second, involvement was in both the ethmoidal cells and antrum on the right side. In the latter instance an orbital abscess complicated the sinus infection and in its contents Torulae were present in pure culture. I have also observed two instances of ulcerative lesions in the oropharynx due to Torula infection,[31] and in another patient there was encountered a filamentous lesion on the dorsum of the tongue due to a chromogenic (brown producing) Torula.[32]

There has also come under my observation an infection of the left tonsil and dorsum of the tongue with Aspergillus niger in a young white man who was free from other disease, and in whom the lesion, while very resistant to treatment, did not extend to other anatomical structures. A single instance of pulmonary aspergillosis has occurred in my practice in a white male 36 years of age. The infection ran a protracted course, but eventually cleared up under iodine therapy.

Infection of the skin of the external auditory canal with various pathogenic fungi gives rise to a condition which has been designated as otomycosis. It constitutes a minor aural disease, and is the type of mycotic infection most frequently encountered in otolaryngologic practice. The condition is widely distributed and is more prevalent in the warm, moist climate of tropical and subtropical zones, but it is a mistake to believe that it is confined exclusively to such areas. The itching ear, in which the canal is filled with exfoliated epithelial debris of caseous consistency, is a familiar picture to most otolaryngologists, regardless of where they are practicing. Heat and moisture have an appreciable effect on the resistance of the skin to invasion and the degree of pathologic change produced by fungi growing within the external auditory canal is greater where climate creates the optimum cultural conditions, but it must be borne in mind that the various fungi producing mycotic otitis externa are capable of growing under adverse conditions with varying degrees of luxuriance.

The usual organisms causing otomycosis are the Aspergilli, the pathogenic yeasts, Penicillia, and the Mucoraceae. The condition is easily recognized. Examination of smears from the affected ear will often give a definite clue to the nature of the disease, but exact classification of the infecting fungus is possible only by cultural studies. We have found slide cultures of great service in this respect, as the type of organism is usually easily identified, and, in addition, the flat surface on which they grow will enable one to obtain photomicrographs with facility.

The symptoms of otomycosis do not warrant an extended description. Suffice it to say that the sensation of a foreign body in the auditory canal with associated itching, at times intense, are the usual findings. If the epithelial mass in the canal is sufficiently large, hearing may be interfered with. Perforation of the drum membrane attributable to the action of the fungi has not been observed in my practice, and though it has been recorded,[33] it must be of rare occurrence. I have seen myringotomy performed in mycotic infections of the auditory canal due to misinterpretation of the redness of the drum membrane caused by the mycotic process when the debris associated with their growth has been cleared away. This mistake should be easily avoided. Pain is a prominent symptom when deep invasion of the skin of the canal occurs and with the advent of secondary pyogenic infection it is intensified and may become agonizing in its severity.

The presence of cerumen in the ear apparently exerts a restraining influence against invasion with fungi, but this is not always true, for instances have been encountered in which fungi were actually growing on a ceruminous plug.

The sequence of pathologic events in otomycosis is somewhat in the following order:[32] Implantation of the organism on the epithelium of the external auditory canal occurs which is followed by a dormant stage which varies from a few days up to two weeks, when the stage of proliferation comes on and the fungus grows actively with associated irritation of the superficial layers of epithelium in the canal which, if it progresses further, becomes an actual inflammation in which the top layers of epithelium are exfoliated and mix with the mycotic growth to produce the mass of debris characteristic of otomycosis. It is in conjunction with this state of the pathologic picture that itching is a prominent symptom and is attributed to the action of the infecting fungi and the toxins which are elaborated in their growth. If the infection is not brought under control, penetration of the subepithelial structures takes place, usually in conjunction with secondary pyogenic invasion which gives rise to suppuration manifesting itself as a pyogenic dermatitis, furunculosis, or perichondritis. The cartilaginous portion of the ear may become involved and marked destruction follow. In the suppurative stages pain is present which is often sufficiently intense to require narcotics for its

relief. Ulceration of the infected areas may occur where the integument is subjected to the action of macerating secretions. Long-standing fungus infections of the ear produce thickening or lichenification of the skin and eczematoid changes may supervene. Extension onto skin surfaces often takes place and may become widespread. I recall several instances where a mycotic dermatitis of the face and neck was due to extension of infection from a mycotic ear. Such conditions result from improper treatment, neglect of treatment or failure to recognize the true nature of the condition from which the patient is suffering. Cicatricial changes follow in the wake of the more severe mycotic infections of the ear and the subsequent contraction of cicatricial tissue may give rise to discomfort in the involved area which is most rebellious to treatment. The patient with otomycosis does not necessarily run the entire gamut of pathologic events noted above as proper treatment will arrest the progress of the disease at any point in its course.

The differential diagnosis of mycotic infections in general may present a perplexing problem and may not be evident until the necessary laboratory reports are rendered. Cultures made from areas suspected of being mycotic in nature should not be discarded or reported negative until a two weeks period has elapsed, for many of the fungi do not grow rapidly and may be missed entirely unless this point is observed.

Prognosis.—The principal danger in most mycotic infections is that of extension from the primary focus to the deeper organs, such as the lungs, or other viscera, and, as is often the case, the central nervous system. This is particularly true in mycotic lesions involving the mucous membranes of the respiratory tract. Early and vigorous treatment of the initial focus may result in saving the patient's life by eliminating the danger of systemic involvement.

In certain mycoses reinfection may occur. This is particularly true in the types which involve the ear. Mycotic otitis externa, while not dangerous to the patient's life, is a source of much annoyance and discomfort. In this condition reinfection is frequent. In certain regions it is almost axiomatic to say that the reopening

Table 1

DIFFERENTIAL FEATURES OF YEAST, TORULA, OIDIOMYCES, MONILIA, AND COCCIDIOIDES

(Modified from Stoddard and Cutler and Shapiro and Neal)

	Genus	Reproduction	Sporulation	Mycelium	Sugars
Fungi Imperfecti — Blastomycetes	Saccaromycetes	Buds	Ascospores	Absent	Fermented
	Torula	Buds	Absent	Absent	Usually not fermented. Varies with concentration of carbohydrates
	Monilia	Buds	Absent	± (variable)	Fermented
	Oidia	Buds	Absent	Present	Not fermented
	Coccidioides	Never buds	Endospores present	Present with aerial hyphae	Not fermented

Pathogenicity	Lesions	Pathologic Characteristics	Size of Organism in Microns
Feeble	Skin, mucous surfaces	Necrosis; epithelial overgrowth; giant cells; abscess formation; polymorphonucleosis	...
Moderate	Nervous system; other organs to less extent; skin rarely, mucous membranes of respiratory tract	Chronic inflammation; caseation occasional; polymorphonucleosis slight or none unless secondary invaders present; gelatinous matrix, acute nodular or ulcerative lesions on mucous surfaces	1-13
Moderate	Mucous membrane: mouth and gastro-intestinal tract; slight skin pigmentation	Chronic ulceration, semi-translucent membrane formation on mucous surfaces	5-10
Slight	Skin always; often bones, internal organs and brain, mucous membranes	Necrosis; epithelial overgrowth; miliary abscesses; tubercle-like nodules; polymorphonucleosis; no gelatinous matrix; membrane formation	3-30
Marked	All organs; often skin	Nodules and cysts; giant cells; caseation; abscess formation; polymorphonucleosis; no gelatinous matrix; granulomatous skin lesions	5-85

of swimming pools is a harbinger of the mycotic ear infections of the warmer months.

Treatment.—In all mycotic infections which have become generalized and in most of the local lesions, the treatment is essentially the same and consists in the use of iodine or the iodides, in conjunction with some form of radiant energy such as the x-ray. Clerf[34] and New[35] have used this therapeutic combination with a measure of success in laryngeal blastomycosis and in our hands it has been effective in treating local lesions of the mucous membranes of the oropharynx caused by Torula, Monilia and Aspergillus. Our results in treating leptothricosis of the tonsil by these measures have not been encouraging.

In general, iodine and iodine-bearing preparations are favored by most writers on mycotic infections of the air passages. Antimony and potassium tartrate has been utilized with indifferent results. Colloidal copper has produced favorable response in the hands of certain observers. Radium which has been tried by many observers has not, in my experience, measured up to the effectiveness characteristic of x-ray. The latter has the additional advantage of being somewhat more economical, and is readily available to the average patient.

In certain mycotic infections such as torulosis, moniliasis and coccidiosis, vaccines or filtrates from cultures of the responsible organisms have been used with varying degrees of success. My personal experience with vaccines in mycotic infections has been limited, but the impression has been gained that they possess a definite degree of effectiveness and should be employed as an adjunct to other forms of therapy, particularly where the infection has proven resistant to the usual forms of treatment. Regardless of the type of therapy employed in treating generalized mycotic infections, it is imperative that it be employed as early as possible in the course of the disease and vigorously applied. There is no form of treatment known to medical science which will overcome the constitutional involvement of mycotic infections in their terminal stages. It, therefore, becomes imperative to make an early and exact diagnosis of mycotic diseases and to apply unrelentingly such measures as we have at our disposal to bring them under control. This is especially true when the infection exists only as a local lesion.

In the therapy of otomycosis, the measures employed are relatively simple and, if properly carried out, are productive of results which are entirely satisfactory. A great variety of fungicides and fungistatic preparations have been employed in the treatment of this condition, some of which exhibit a marked degree of effectiveness, while others are practically without value. King Gill[36] was first to call attention to the high degree of clinical effectiveness of metacresylacetate in otomycosis. McBurney and Searcy,[37] in a recent article, have confirmed his observations and have pointed out the fact that many preparations are in common use in the treatment of otomycosis which have little or no therapeutic value. Their conclusions were based on experimental as well as clinical investigation. They conclude that metacresylacetate or cresatin heads the list in degree of effectiveness as a fungicide in otomycosis, and that its therapeutic value is slightly enhanced by the addition of thymol. In our experience, the order of clinical effectiveness is as follows: (1) metacresylacetate or cresatin, (2) tricresol in glycerine, (3) Castellani's solution,* (4) iodine in petrolatum or boric acid powder, (5) phenyl mercuric nitrate 1/3000 alcoholic solution, (6) copper salts, such as copper sulphate, chloride, and oleate. We have tried thymol in several combinations, and while it apparently ranks high in fungicidal power, many patients object to the burning sensation which its application causes. A combination of tricresol 1 per cent, iodine 2 per cent and thymol 1 per cent in boric acid powder has a definite field of usefulness in the terminal stage of treatment of otomycosis when the use of a powder by insufflation is advisable.

The essential points in the treatment of otomycosis are: first, the control of pain; secondly, the control of the mycotic infection; and thirdly, the prevention of reinfection. Quite often the external auditory canal cannot be adequately cleansed on the patient's first visit to the physician, because of the pain which manipulation causes. It is in such instances that metacresylacetate serves a twofold purpose, as local analgesic and as a fungicide. A cotton wick saturated with this drug can be inserted into the depths of the canal and kept moist by reapplication of the drug at intervals. It is usually advisable to add a vegetable oil, such as olive oil, to the prescription which the patient is to use in this manner, as pure metacresylacetate may cause undue exfoliation of surface epithelium. The wick referred to above is removed from the auditory canal in twenty-four hours, at which time the surface epithelium

*Castellani's solution is a saturated alcoholic solution of basic fuchsin to which 10 per cent resorcinol has been added. It also contains phenol, boric acid, and acetone.

will be white in appearance and loosened, so that it may be easily removed by swabbing. Occasionally it is necessary at this point in the treatment to remove epithelial debris by irrigation. Knowles[38] has found gentle blowing of compressed air through a small bent metal tube to be of service in the cleansing process.

Occasionally recourse may be had to irrigation with water, but the introduction of water into the auditory canal in mycotic infections, unless it is carefully removed after it has served its purpose will stimulate the growth of fungi and often causes an increase in symptoms.

After the second or third application of metacresylacetate on a cotton wick, the canal can usually be adequately cleansed, and it is usually advisable to change to some other preparation such as iodine in petrolatum, or some of the fungicides noted above. When eczematous changes are present in addition to the mycosis, they will require additional treatment which is carried out along the usual well recognized lines.

When pyogenic involvement is present as a complication, attention must be given to this through additional measures such as vaccines, local heat, bacteriophage when adaptable, and sedatives for the control of pain. Incision into infected tissue is not often required and when contemplated should be undertaken with caution, as extension into the cartilage of the ear may give rise to troublesome consequences. When the *Bacillus pyocyaneus* is present as a co-infecting organism, 2 per cent aqueous solution of acetic acid is recommended as an application, as it renders the epithelium unfavorable for the growth of this organism.

Prevention of reinfection is important, and if swimming is indulged in, the ears should be carefully dried afterward and 70 per cent ethyl alcohol instilled into them as a prophylactic measure.

Where radiant energy, such as x-ray and radium, are employed in the treatment of otomycosis, one should not overlook the suppressing effect which these agents have on the ceruminous glands in the skin of the external auditory canal.

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DISCUSSION (*Abstract*)

Dr. H. B. Searcy, Tuscaloosa, Ala.—Numerous classifications of the fungi are found in literature, but there has been very little in the line of treatment. I appreciate Dr. Gill's mention of my work in otomycosis, but am sorry that he could not substantiate my findings with the use of thymol. The iodides have been the recognized internal medication for too many years and no advance has been made along this line. A generation or more ago syphilis was diagnosed by a therapeutic test of giving potassium iodide. If the

patient got better our fathers called it syphilis, just as quinine was used as a therapeutic test for malaria. I am sure that many cases of mycosis was called syphilis. I now have five cases of actinomycosis of the jaw which cleared up nicely with thymol medication internally and 10 per cent thymol in olive oil injected locally into the fistulous tracts. All these cases were supplemented by the use of potassium iodide or tincture of iodine internally. One patient has been well now for 10 years. I do not hesitate to prescribe thymol in 5 grain capsules followed by a glass of milk to assist in absorption, at the ratio of 10 grains of thymol per 100 pounds of body weight.

Locally, in mycosis of the external canals I still use 1 per cent thymol and whatever antiseptic or vehicle is indicated, as alcohol, olive oil, various salves, or boric acid powder. My results warrant my continuing this line of treatment.

When a drying mixture is indicated, I like thymol in merthiolate and alcohol. When an oil is indicated, I add 1 per cent thymol to cresetin, usually diluting cresetin with olive oil. When a powder is indicated, I add 1 per cent thymol to 1 or 2 per cent iodine and boric acid powder.

HIGHLIGHTS OF THE HISTORY OF OPHTHALMOLOGY*

By Wm. Thornwall Davis, M.D.
Washington, District of Columbia

The story of ophthalmology may be divided into five parts:

(1) The beginnings
(2) From Hippocrates until the Middle Ages
(3) The Middle Ages
  Byzantine
  Saracenic
  Western Middle Age
(4) The modern period: Europe
(5) The modern period: America

(1) *The Beginnings.*—The earliest mention curiously enough is in a law code; the Code of Hammurabi, 2250 B.C., a collection of laws enforced by a king of Babylon. Medicine at this period was entirely in the hands of the priests and hence was mostly theurgy and magic. The earliest records of ophthalmology are in the Brugsch and Ebers Papyrus. The latter is the more important. It was purchased by the Egyptologist Ebers from an Arab who discovered this papyrus between the legs of a mummy in the necropolis of Thebes. It is in the library of the University of Leipsic. It consists of 110 pages or columns describing all the diseases known to the Egyptians at this time. Eight pages are devoted exclusively to diseases of the eye. The ophthalmic portion of the papyrus was translated into German and published at Leipsic. A translation of the whole papyrus was published in Berlin in 1890.

Some of the more important ocular diseases and remedies were as follows:

For "blood in the eyes," which meant red eyes from any cause, subconjunctival hemorrhage, ecchymoses, conjunctivitis, and so on, the remedies were verdigris, antimony and powdered wood. Tear eyes or watering eyes were treated with boiled papyrus, acacia gum, antimony and water.

For dimness of sight, swamp water, compresses of antimony and honey were used. A favorite prescription was honey mixed with the excrement of a child.

Trachoma was then as now widely spread and was a terrible curse.

For turning of the eyes (strabismus) equal parts of tortoise brains and oriental spices were used.

Among other diseases mentioned are bade, conjunctival edema, pus in the eyes, mounting of water in the eye (probably cataract), swelling of the nose (dachryocystitis), curving of hairs into the eye, trichiasis). The doctors were priests and *vice versa.* Later this changed and the two professions separated. Nothing was known of anatomy at this time nor was known until the Seventh Century B.C., when it was investigated by the Greeks.

The ancient Egyptians thought that most diseases were engendered by worms or excessive eating. They practiced inspection, palpation, auscultation, percussion and examined the urine. These methods were of course rudimentary.

Most of the Papyrus Ebers, however, is devoted to therapeutics. There was considerable rational therapeutics, but mostly it was mixed with the grossest superstition. The earlier the manuscript the less the superstition; the later, the more admixture of magic; an interesting commentary upon the decline of Egyptian medicine. Emetics and purgatives were employed. The enema seems to have originated with the Egyptians. Bleeding was commonly resorted to. Diuresis and diaphoresis were also used. They also employed powders, salves, poultices, gargles and suppositories. Medicaments were onions, castor oil, pomegranate, copper salts, hemoch and opium. Circumcision and castration were performed.

It was mostly in hygiene, however, that the Egyptians contributed to medicine. Over-eating was practically unknown. There was a good system of meat inspection. There were innumerable rules, mostly sensible, relating to the bath, clothing, sexual intercourse, and so on.

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*From the Department of Ophthalmology, George Washington University School of Medicine, Washington, District of Columbia.

Later came abundant specialization and with it came the period of decay and gross superstition and idiotic magic.

Greek Medicine.—In the Iliad we read of the rational treatment given wounds during the Trojan War and of powders and poultices given to arrest hemorrhage and alleviate pain. Opium was known to the Greeks at this time. There was considerable mysticism attached to medicine. Some thirty gods were called upon for various illnesses. Venesection was old even in this ancient time.

Chiron the Centaur was the preceptor of Aesculapius (Roman) or Asclepius (Greek), the greatest of all the gods of healing. He was supposed to be the son of Apollo by the nymph Coronis. Temples were erected to Aesculapius usually in a salubrious situation and near thermal springs. Regular corps of priests officiated in these temples and formed schools for giving medical and surgical instruction. Two sons of Aesculapius became surgeons of reputation, Machaon and Podilirius. Afterwards the Aesculapian temples became hospitals where the patients remained and were treated. There was considerable trickery practiced: impersonation of the gods by the sacerdotal personages; acoustic arrangements whereby the deity was supposedly heard in the room; large non-venomous snakes were kept in these temples and glided about at will. Aesculapius was supposed to assume the form of a serpent whenever he appeared to mortal eyes. Two of the best known of these temples of medicine, the forerunner of the hospital as we know it, were the Asclepirion at Athens and Hieron at Epidaurus. There is little information in Greek literature concerning these temples. Some of the priests in these temples were known as Asclepiades, sons of Aesclepius. They claimed physical descent from the god. They separated themselves from the remainder of the Aesculapian priesthood and became independent physicians. Thus there became three classifications of physicians:

(1) The priests in the temples of Aesclepius.

(2) The Aesclepiadae, no longer connected with the temples, but claiming descent from the god.

(3) Independent physicians in whose history there had been no temple connection.

There were state physicians on a salary. State medicine hence was present before the time of Hippocrates. There were also military and naval surgeons and physicians to the courts of kings and princes.

The Aesclepiadae were rational physicians; that is, they were unconnected with superstition and fraudulent practices of the priests. Secondly, they were educated and broadly qualified men. From these men modern medicine is said to have originated. It is said the Hippocratic oath, as we know it, was originated by this group before the advent of Hippocrates.

Hippocrates the Great was so-called because there were many Hippocrates. He was born on the island of Cos. Here was one of the great medical schools of the day. He was the son of the Asclepiad Heracleides and was presumed to have descended through his father from Asclepius and through his mother from Hercules. He traveled throughout Hellas, Asia Minor and Egypt. He also studied in the rival Greek School of Medicine, the Cnidian. He lived in the Golden Age of Greece at the time of Pericles, Socrates, Thucydides, Sophocles and Euripides. It is no wonder that the great art of medicine flourished then.

We think of Hippocrates as having written the Corpus Hippocraticum. This is supposititious. Many were engaged in the writing of this book. So far as we know, Hippocrates the Great wrote but six books, but in these books is the spirit of modern medicine and ophthalmology. It is intertwined with Greek philosophy, the liberator of the human intellect, from the tyranny of superstition and magic. It dealt with ethics, the relation of man to man and with manifestations of the physical world, natural science. The germs of this philosophy came from Egypt, India and China and fell upon rich ground.

Pythagoras it was who discovered the optic nerve.

Socrates was a contemporary of Hippocrates and exercised a deep influence upon him. This was about 500 B.C. Socrates was not a teacher, but spent his life in influencing the minds of his countrymen by his pure life and high intellect and culture. His life was nearly perfect, so much so that he has been compared in this respect with Christ.

Socrates desired to cure diseased minds, Hippocrates to cure men's physical infirmities and thus founded practical scientific medicine. Hippocrates was a meticulous observer of the phenomena of disease without regard to how it might appear to demons or gods. He possessed the inquisitive senses of a child, the brain of a scientist and the heart of a philanthropist.

The Hippocratic Collection was compiled and edited about 300 B.C., the Alexandrian era, in

Alexandria, and is known as the Corpus Hippocratium. Hippocrates was such a keen observer that the unscientific pathology of this time did not pervert his judgment. He employed all his senses in the detection of disease; the pity of it today that they are so neglected. He took the anamnesis carefully, and more pity that this, too, is neglected today. He noted the prognostic value of strabismus, proptosis and inequality of the pupils in the acute infections. He often prescribed specific diet, bathing, exercise and massage, remedial agents which even now are much neglected by our profession. He antedated Hahneman in the principle that like cures like, in that he observed that disease could at times be cured by a drug that produced the symptoms of the disease in question. He was an extremist in nothing, and this we might indeed well ponder in our medicine of today. Neuberger says of him:

"His diagnosis and treatment of diseases and treatment of the osseous system serves as a pattern for all time."

He had some dim knowledge of asepsis and antisepsis and knew healing by first and second intention.

A general statement of what he accomplished in medicine might be as follows:

He separated scientific medicine from temple medicine.

He cast away theurgy and magic.

He introduced the science of observation and inductive reasoning.

He instituted the wholesome doctrine that the physician, while doing enough, should never do too much.

He recognized the ophthalmias, pterygium, chalazion, ectropion, trichiasis, ulcers and scars of the cornea (nystagmus) and photophobia.

Restricted diet and hot applications were prescribed as were preparations of copper, iron and lead.

He treated trachoma by rubbing the inner surface of the lid with wool wound upon a stick of wood, followed by cauterization of the surface so treated. This was followed by collyria of salts of copper. We have not improved upon this treatment.

He treated night blindness with ox liver!

Aristotle was the first to describe the iris and to note that all children are born with blue irides. His conception of color vision was incredibly like that of today. He knew of errors of refraction and the failure of accommodation in later life, though he did not know the causes.

Alexander, an apt pupil of Aristotle, conquered Egypt in 332 B.C. and Hellenized it in part by building the city of this name. The great library, the center of learning of the world of that day, was built by Ptolamy Soter, one of Alexander's generals. In this great university, ophthalmology was highly cultivated, though we have but little knowledge of the details. Herophilus, the founder of human anatomy, described and named the retina, the uvea, the vitreous humor and the ciliary processes.

Roman and Alexandrian medicine was Greek medicine transplanted. The Roman, Celsus, is the author of the oldest systematic treatise on ophthalmology which has come down to us. It dated about the time of Christ. In it he discusses many diseases of the eyes and the treatment therefor. He practiced depression of the cataract. His is probably the greatest ophthalmic writing of antiquity until the time of Galen. Pliny said:

"There is also no law against incompetency (in medicine). * * * The doctor is the only person not punishable for murder."

He speaks of the moon's influencing the disease of the eyes of beasts of burden, no doubt the moon blindness of the horse of today, which we know now to be a low-grade uveitis of unknown etiology.

Galen, A.D. 131, of Asia Minor, physician to Emperor Marcus Aurelius, may be regarded as the greatest physician of all ages next to Hippocrates. The ocular anatomy and physiology of Galen is the culmination of these subjects in all antiquity and nothing of great worth was added to them for 1,600 years.

Medicine during the time of the Roman Republic was looked upon as a trade and held in contempt. It might be well for us at this time to contemplate this fact.

During this period there was extensive specialism, particularly ocular. Following this period, the fall of the Roman Empire, came the Middle or Dark Ages. These may be geographically divided into the Byzantian, Asia Minoran and Roman. The best known man of this geographical group was Aetius of Amida. The Arabic or Saracenic (Middle Ages), best known writer on ophthalmology, was Rhazes. This comprised Arabia, Persia, Syria, Egypt, and Spain.

In the Western Middle Ages, the best known men were Roger Bacon and Leonardo de Vinci, and this comprised more particularly Italy, France, and England.

It should be observed that these groups are purely geographical for the purpose of arrangement and the men spoken of belong to the Middle Ages.

Aetius was scientific for his time, but lapsed into the superstition of the time on occasion. His work, grouped as Tetrabiblon, so far as ophthalmology is concerned is a perfect complement to the optics, anatomy and physiology of the eye as presented by Galen. The writings of Galen and Aetius, when considered together, form a complete ophthalmology of antiquity.

Paul of Aegina, famous surgeon, obstetrician and ophthalmologist, studied at Alexandria. To him we owe the condensation of the medical collections of the great library. He also set aside this work in the nick of time to save it upon the burning of the manuscripts of the library by the Mohammedan General Amror.

It is a strange and interesting circumstance that from the depths of the desert about 630 A.D. arose an unexpected force, Mahomet, believing himself a prophet of the one and everlasting God. This so consolidated the peoples of this and other regions that they conquered and overran Arabia, Persia, Syria, Egypt, North Africa and Spain. It seemed that they were about to conquer Gaul, Germany, Italy, England and the whole of Europe when the tide of invasion was held back by the genius and energy of one man, Charles Martel. This leader with his men at the battle of Tours slew 375,000 Arabs, which stemmed the invasion.

It will be recalled that Constantinople finally fell to the Turks, Mohammedans, near the close of the Middle Ages. These historical facts are repeated to show the effect upon science and hence upon medicine. The Saracens burned the famous library at Alexandria, causing a hiatus between the ancient and modern era which cannot be bridged. The great compendium of medicine by Paulus of Aegina was composed of seven books and was the authority in medicine throughout the Byzantine Middle Age and the whole of the Saracenic or Arabian period. It was spoken of by the Arabs as the Collection of the Pleiades, in allusion to the seven brilliant books. Of these seven books, Book I deals with Dimness of Sight; Book III is on Diseases of the Eye; Book IV on Burning the Head for Ophthalmia.

The Saracens, even though they destroyed the Alexandrian Library, later became the saviors and purveyors of the sciences through these dark periods. Rhazes, discoverer of the pupillary reaction to light, was the exponent of this period. He was like Hippocrates, a true reasoner and close observer. He was educated at Bagdad. The passage from his "Continens," an encyclopedia of medicine of its day, regarding the pupil is interesting:

"In the middle of the icy (iris) humor appears a hole which now dilates and now contracts according as the icy humor feels the need of light; it contracts when the light is strong and dilates in obscurity. The hole is the pupil and the membrane the uvea."

A number of monographs in addition to this "Continens" were written by Rhazes.

(1) Why the pupils contract in the light and dilate in obscurity.

(2) On the matter of vision: wherein is shown that the eyes are not radiators of light.

(3) On the conditions of sight.

(4) On the form of the eye.

(5) The book of the surgical treatment of the eye, etc.

Ali Abbas, in the Tenth Century, contributed as his chief work in medicine "Al-Maliki: The Kingly Book," since it was dedicated to the Emir.

The most distinguished of Arabian oculists was Abdul Quasim Ammar, inventor of the suction operation for cataract. The most distinguished physician was Avicenna, known as the Prince; a wealthy, highly educated and cultured man who finally became Vizier in Hamadan.

The Arabian mathematician Alhzea contributed much in the field of physiological optics. He might be styled the father of geometric and physiologic optics.

The Western Middle Ages.—About 1050 the Seljukian Turks, warlike Tartars, cruel beyond belief, conquered the Saracenic Arabs. Then began most horrible persecutions of Christians. This provoked a maniacal wave of religious frenzy in Western Europe. The preaching of the fanatic Peter the Hermit was the result, and he was father provocator of this fanaticism. Then arose the Crusades, the first four being titled the Principal Crusades, the second four the Minor ones. Among numbers of other expeditions the most insane of all was the Children's Crusade, originated by a French boy 12 years of age. Most of the children were lost in the Mediterranean. Many were sold in Tunis, Alexandria and other Mohammedan slave markets.

But travel liberalized the minds of the soldiers of the cross and some of the Arabian learning penetrated the West, that is, Europe, particularly through the mind of the celebrated

monk, Constantinus Africanus. He it was who coined the term cataract.

The greatest scientist perhaps in the Western Middle Ages is Roger Bacon, the first to suggest the use of lenses to correct vision. He was born in England in 1214. There is no authentic information that lenses were known of or used before this. Bifocal spectacles were invented by Benjamin Franklin. Cylindrical lenses were first used about the beginning of the Nineteenth Century. Near the middle of the Ninetenth Century, owing chiefly to the efforts of Arlt, the correction of refractive errors and fitting of glasses was done by ophthalmologists.

Leonardo de Vinci was a famous Italian painter, sculptor, architect, musician, engineer, optician and physiologist and the producer of Mona Lisa. He it was who discovered that the retina and not the crystalline lens is the organ of vision. He is thought by some to have discovered the principle of the camera obscura and to have applied this knowledge in the explanation of the optics of the eye.

THE MODERN PERIOD OF OPHTHALMOLOGY: EUROPE

We must give a moment's consideration to science as a whole at the beginning of the modern age. Gunpowder had been invented with its far-reaching consequences. The mariner's compass and the astrolabe had been devised. Paper was invented in the Tenth Century. The Arabs had contrived the numerals of today and also algebra and other divisions of mathematics and had contributed much to the science of chemistry.

The degree "Doctor" in its present meaning began to be conferred in the Twelfth Century. Clocks were invented in the Fourteenth Century. Printing with its boundless possibilities and consequences caused the diffusion of this knowledge and our present civilization was on its way.

The Sixteenth Century was full of advances in all branches of science and medicine and literature: Copernicus, Shakespeare, Vesalius, Fallopio and Eustachius; the three latter the reformers of anatomy; Paracelsus the quack, yet with great ability; Paré, the great force in surgery and obstetrics; Leonhart Fuchs, a distinguished botanist and general practitioner of Bavaria, wrote of ophthalmology. He is not to be confused with Ernst Fuchs, of Vienna, of a later date.

Ambroise Paré, 1509, first studied in a barber shop, then in the Hotel de Dieux. He is spoken of as the father of modern surgery and did much to advance ophthalmology.

George Bartisch is the father of modern ophthalmology.

The Seventeenth Century brought forth such men as Acquapendente, who showed the correct anatomic position of the crystalline lens.

Ruysch first described the arteria centralis retinae and the venae vorticosa.

Meibom, for whom the Meibomian glands are named, described but did not discover them, since they were known to Galen.

Van Leeuwenhoek discovered the rods of the retina, the fibers of the lens and cornea and the epithelial layer of the latter.

Benoist Daca da Valdes, not a physician or apothecary, was a licentiate and notary. He published, however, in 1623 a work of 100 pages on the use of spectacles and what strength to prescribe for different ages in presbyopia.

Johannes Kepler, 1571, advanced the science of optics more than any one up to the time of Helmholtz.

Sir Isaac Newton, discoverer of the law of gravitation, also discovered the dispersion of light, the composite nature of white light and the unequal refrangibility of different colors.

Father Schoermer, Jesuit Priest, aided greatly the knowledge of optics. He studied the indices of refraction of the media of the eye, measured the curvature of the cornea and demonstrated the inversion of the retinal image.

Mariotte, the famous French physicist, discovered the blind spot which bears his name.

We come now to the Eighteenth Century and the mosaic of knowledge laid down in the previous 5,000 years was increased and diffused more than in all the preceding centuries. The outstanding ophthalmological event in this century is the extraction of cataract. Petit, of Paris, showed that soft cataract could be removed by discission and demonstrated the circumlental canal that bears his name.

Jacques Daviel, France, 1696, was the first to extract a cataract in the modern sense. There was sharp dissension among the ophthalmologists as to the value of the procedure. It was not accepted by the profession as a whole for many years.

To the Nineteenth Century belong tremendous advances in science and medicine, anesthesia and surgical asepsis probably being the outstanding advances.

In ophthalmology came ophthalmic hospitals, journals, professorships, societies, textbooks, refraction and the ophthalmoscope, which opened a new world no less than the biomicroscope or slit lamp. The first professorship in ophthalmology was founded in Paris in 1765. In 1773 a like foundation took place in Vienna.

The first public hospital for eye and ear work exclusively was the Royal London Ophthalmic Hospital (Moorefield's) founded in 1805. In 1807 it was restricted entirely to eye diseases.

The first ophthalmic society was an international one and was the first international medical meeting of any kind. It met in Brussels in 1857. The first local ophthalmological society was the Heidelburg one founded by Von Graefe in 1863.

Germany gave the Nineteenth Century most of its textbooks. Arlts Kranukheiten des Anges, in 1856, and later Ernst Fuch's Lehrbuch der Augenheilkunde were the outstanding books. The last named was translated into English by Duane and is even today, for the moment perhaps, as good as any we have, though rapidly becoming obsolete.

Perkinje discovered the images which bear his name, the reflection of a great image on the cornea and anterior surface of the lens and an inverted image on the posterior concave surface of the lens. The changes in the curvature of the crystalline lens were thus clearly demonstrated.

Sir William Bowman discovered the ciliary muscle (muscle of accommodation) in 1847, which solved the confusion on how accommodation takes place. As a matter of fact, it is not entirely understood yet.

The motor apparatus of the eyes was studied by Muller in 1823, Volkman later. Maddox, Stevens, Claude Worth and Savage of Nashville, Tennessee, have contributed much to this intricate study. There is a wide field as yet to be explored. Savage was well ahead of his day and remains so yet. Like many who think ahead of their fellows, they are subjected to ridicule from the shallow and superficial minds of their time.

Perimetry is largely a Nineteenth Century development. Boerhaave wrote a little on this subject. Thomas Young was the first to develop the matter scientifically. This was emphasized by the great German ophthalmologist, Albrecht Von Graefe, and he was followed by Foerster with the first perimeter.

Helmholtz brought forth the ophthalmoscope in 1851.

Babbage in reality invented this instrument seven years before Helmholtz, but did not report it.

Himly introduced mydriasis in 1801, which advanced us much in the study of the fundus oculi.

Jaeger, of Vienna, introduced the test cards in 1854 which bear his name. Snellen gave us the test letters for measuring the visual acuity for distance.

Donders gave us the greatest work on refraction which we have been unable to add much to as yet.

Sir William McKenzie gave us the greatest treatise on glaucoma in 1830.

Von Graefe gave the world the operation of iridectomy in 1856 for the cure of glaucoma. Later in the century Elliott described sclerocorneal trephining. Dalton, a physicist and chemist, called attention to and began the study of color blindness in 1794. Sixty years later the study of this condition was taken up by young Helmholtz and others.

Hutchinson brought out his study in 1862, when his "triad" of syphilitic teeth, labyrinthitis and interstitial keratitis became a classic.

The x-ray was first used in ophthalmology by Dr. F. H. Williams, of Boston. Further contributors to this science were deSchweinitz, Sweet and Oliver. Credé's method of prophylaxis against gonorrheal ophthalmia was advanced in 1884.

Atropin was isolated in 1831 by Mein and was shortly afterward used in ophthalmology by Osler.

Refraction was studied by many and suddenly assumed a scientific basis in 1854, when Helmholtz's work, "Textbook of Physiological Optics," came out in 1864 and when Donders brought out his great work on "Refraction and Accommodation of the Eye."

AMERICAN OPHTHALMOLOGY

Dr. Elisha North was the first American of importance in this work and established the first ophthalmic infirmary at New London, Connecticut. Dr. George Frick, of Baltimore, published the first work on ophthalmology in the

United States. He studied in Vienna under Beer.

The first separate course of clinical lectures on ophthalmology were by Dr. Henry Ward Williams, of Boston, at the Harvard Medical School in 1850. He, with others, formed the first ophthalmological society in 1864.

Isaac Hays, A.B. University of Pennsylvania, and M.D. Yale, 1820, reported the first case of astigmatism observed in the United States and the first case of pathologic (not congenital) color blindness.

William Gibson, A.B. Princeton, 1809, M.D. Edinburg, was the first in history to perform an operation for strabismus in 1818. William Edmonds Horner, discoverer of Horner's muscle (tensor versi), was born at Warrenton, Virginia.

Drs. Edward Reynolds and John Jeffries established an eye dispensary which developed into the Massachusetts Charitable Eye and Ear Infirmary.

Dr. Samuel Gross was widely known as an eye operator. His graduation thesis was "The Nature and Treatment of Cataract."

Dr. Charles Alfred Post wrote a tiny book in 1841 titled "Observations on the Cure of Strabismus."

Joseph LeConte, physiologist, naturalist, general practitioner and ophthalmologist, M.D. College of Physicians and Surgeons, practiced in Macon, Georgia. He was a chemist in a Confederate laboratory. In his volume entitled "Sight" he gave the fullest and most adequate description and treatment of binocular vision recorded to this date.

Agnew, Gradle of Chicago, Hotz, Hildreth, Jacobson, Herman Knapp of New York, John Green of St. Louis, Martin Hayward Post of St. Louis, Hasket Derby of Boston, Aaron Friedenwald of Baltimore, Calhoun of Atlanta, Loning Norris of New York, and Gruening of New York, are some of the outstanding names in the wonderful development of American ophthalmology. Within the past half century or less and more particularly since the World War, when Vienna and other European centers were impaired perhaps in their efficiency, America has advanced in instruction and knowledge of ophthalmology.

I think it can be said that the student can obtain as good and possibly better training in ophthalmology in Boston, New York, Philadelphia and Baltimore, as well as other places over our country, as he can anywhere in the world. Barring national cataclysms from war or worse fates, America is probably due to lead the world in ophthalmology and is actually doing it.

The newest operation which has startled the ophthalmological world is the micropuncture method of treating detached retina.

The biomicroscope and slit lamp has opened up as great a new field as did the microscope and ophthalmoscope.

927 Farragut Square, Northwest

DISCUSSION (*Abstract*)

Dr. J. W. Jervey, Greenville, S. C.—This is a delightfully interesting and informing picture of the "Highlights in the History of Ophthalmology" that Dr. Davis has given us. Here we trace with simple wording and an astute selection of facts and personalities the development of this specialty; and what is more, from every page leaps the bright but gentle spark of sympathetic understanding. Back we go to almost prehistoric times to find out, as a famous modern wit once said, referring to another matter, that this history undoubtedly had its beginning dating in B.C., or if not, then prior to that time. And, lest we forget, it was about 1000 B.C. when King Solomon uttered the immortal words: "Where there is no vision the people perish".

Dr. Davis brings us up by graceful allusions to the time when medicine, including ophthalmology, flourished in the days of "the glory that was Greece and the grandeur that was Rome". He tells us " it is no wonder that the great art of medicine flourished" in the days of Pericles, Socrates, Thucydides, Sophocles and Euripides. Quite true; but though he speaks of "art" he did not mention Phidias or Praxiteles, no doubt because of his natural diffidence, not liking to precipitate a possible discussion of the nude. But he uses the word "art" aptly, for at that time medicine was essentially that, and though science is getting in some sturdy blows, medicine must even today be held as *sui generis* an art. So much for the beginning.

Now, I fear I shall bring a blush to our distinguished essayist's cheeks. From about the First Century (or one might say the last) B.C. to the Thirteenth or Fourteenth of the Christian Era the world has accepted the dictum of historians that the art or science of medicine remained *in statu quo*. Naturally the specialty of ophthalmology was so regarded. But I ask you, gentlemen, and you cannot say me nay, don't you remember the words of the greatest of all teachers, as recorded in the Gospel of St. Luke, when He was speaking to the Pharisees? Singling out one He said—and we can almost see Him shaking His finger in the listener's face—"thou hypocrite, cast first the beam out of thine own eye, and then shalt thou see clearly to pull out the mote that is in thy brother's eye."

That, my friends, is sound ophthalmology today!

And, as an imperishable dictum, why is not that a landmark for all time?

The great philosopher, Ernst Haeckel, once conceived what he doubtless regarded as an aphorism, or even an axiomatic observation: "Nothing is constant but change."

Those five little words are portentous, but obviously they apply only to the physical world. At least some things in the humanities are changeless. History is positive and unchangeable. The spoken word, the deed done, which constitute history, are there, everlastingly impressed on the pages of Time, and could be changed by no conception of the human mind. They may be misunderstood, they may be misinterpreted, but the record of their issue stands forever.

I do not know whether it is that the best minds in the profession cultivate their historical knowledge, or whether the acquisition of such knowledge leads to the development of the best minds. Certain it is, however, that at all times outstanding men like Osler, Welch and many others have been those whose delight was in digging out and perpetuating the salient facts of the history of medicine.

Not long ago I asked a very dear friend, dean of one of the oldest medical schools in this country, this very question, and with only a moment's hesitation he replied: "The best men in the profession take an interest in the history of medicine." Such an interest is a badge of superiority, he meant to say. Having myself an interest in such history, I could not afford to argue the point with him. In either case this explains the high status of our essayist in his chosen specialty.

Dr. Davis points out that Hippocrates used his senses in the diagnosis of disease, and considered the anamnesis, deploring the fact that these aids have largely fallen into disuse. But not so entirely. They are still used in the "provinces" where laboratories are unavailable. And no less a man than Osler impressed upon his students: "Study the anamnesis."

But one more character shows up, which Dr. Davis has not mentioned, in that slumbering sixteen hundred years of medicine, a man who made history in ophthalmology by writing a classic of the time. A few years ago came to my attention Casey A. Wood's translation of Benevenutus Grassus' "De Oculis." It may be that I expected to read something like the stirring exploits of the only other of that name with which I was familiar, Benvenuto Cellini, or his pornographic counterpart, Casanova. But that aside, I read the monograph with the greatest pleasure, and I can only advise you who may be interested in the history of ophthalmology to do the same.

Benevenutus of Jerusalem, whose history is not too clear, lived in the Twelfth Century and, as Wood says in his foreword, he was the "most famous oculist and cataract operator of his day," and a study of his life is "indispensable to a proper understanding of the history of ophthalmology and its progress from the Tenth to the Twentieth Centuries."

I like to think that even if medicine and surgery as a whole were dead for sixteen hundred years, at least there was a practitioner of the specialty to which I have devoted my life who, in the current vernacular, was a "live wire." And he was all of that. Read his book, digest his pronunciamentos, and see and agree.

In all these centuries he was the first to write a book on diseases of the eye, and its printing, the incunable of Ferrara, one of the originals being in the Pierpont Morgan library in New York, is one of the most valuable highlights in ophthalmological history.

As to our essayist's enumeration of the great men in American ophthalmology, I can only say I agree with his ideas and his ideals, but many equally great and brilliant have not been included in his list. Besides, only the passing of time will prove how all or any of these will be evaluated in history. And perhaps some others. Who can tell?

Sic transit gloria mundi!

RECENT DEVELOPMENTS IN THE MATERNAL AND CHILD-HEALTH AND CRIPPLED CHILDREN'S PROGRAMS IN THE SOUTHERN STATES*

By FRANCES C. ROTHERT, M.D.†
New Orleans, Louisiana

The term "recent" will be used in this discussion to include the last two years and the term "southern" to include the area designated as Districts 3 and 4 by the United States Children's Bureau and the United States Public Health Service.‡

The chief development has been a very great extension of both maternal and child-health and crippled children's programs.

Title V, parts 1 and 2, of the Social Security Act, administered by the United States Children's Bureau, authorizes Congress to appropriate funds for grants to the states for the extension and improvement of services for maternal and child health and for crippled children, particularly local services in rural areas and in areas of severe economic distress. However, the extension of these programs has been greater than that provided merely by the appropriations of Congress as authorized under title V, because the strengthening

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†Regional Medical Consultant, Children's Bureau, U. S. Department of Labor.

‡Districts 3 and 4 include Maryland, Delaware, West Virginia, Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Missouri, Arkansas, Louisiana, Kansas, Oklahoma, and Texas.

of related services in general health and welfare fields through appropriations authorized in other sections of the act has directly or indirectly strengthened services for maternal and child-health and for the care of crippled children.

Let us consider first the maternal and child-health services.

The funds provided under titles V and VI of the Social Security Act have acted as a powerful stimulant for health services. State and local appropriations have increased greatly, more than $7,500,000 in the whole United States. Much of this increase was in Southern states, Georgia, Arkansas, Oklahoma, and Texas having been particularly noteworthy.

These appropriations have made possible a great increase in the number of counties having full-time local health service, that is, a service having a medical director, a public health nurse, a sanitary engineer, and an office clerk, all of whom are employed full time. In all the counties in two Southern states and in almost all the counties in another Southern state full-time local health service has been completely organized, and plans are under way for the complete organization of such services in district form in 4 more states. The extension of full-time local health service has provided for a great increase in local maternal and child-health work. Moreover, in areas that do not have full-time local health service there has been considerable extension of health work, partly by means of full-time public health nursing services on a county-wide basis and partly through state-wide services of other types.

These appropriations have also made it possible to provide all the major types of health work in the areas having an organized health service, not only through an increase in personnel (many counties with formerly only one public health nurse now have two or three nurses, and some have even more) but also through the more efficient use of personnel. For instance, there has been a marked increase in maternal-hygiene service—it is agreed that the time to begin building the health of an individual is before his birth. Also, more attention is being given to arranging programs for complete maternal care for the indigent or for families having a low income. These programs include prenatal nursing care and medical care in clinics or conferences, delivery nursing care, and postpartum medical and nursing care. Group instruction is receiving considerable emphasis not only because it reaches more people but also because it offers an educational advantage, in that it permits the exchanging of information between the individuals of the group. More attention is being paid to infant hygiene; the old-time summer round-up is being superseded by continuous supervision of the child from his infancy until he reaches school age. This supervision is taking the form of examinations given periodically throughout the year in child-health conferences or in the doctor's office. School health work is being given proportionately less time in the total program, attention being focussed not on the inspection of every child every year, but on the correction of conditions causing ill health and on the thorough examination of all children who most need examination. Several states are giving considerable thought to the correlation of health education in the schools with the program of the state department of health.

Every Southern state now has a full-time medical director of maternal and child health or has plans for obtaining one. The chief function of these directors in the Southern states, where there is much full-time local health service, is the providing of direction, consultation, and other assistance to the local full-time health officers so that they may follow the best methods of carrying on maternal and child-health services. This involves responsibility for selecting and distributing the educational materials used; formulation of standards of program and of performance in cooperation with the directors of the local health services and of public health nursing; and the provision of a continuous staff-education program in pediatrics, obstetrics, and maternal and child-health methods for the directors of county units by means of frequent consultation visits to the counties and by group conferences. He also gives medical direction in the development of medical conferences in counties having only public health nursing service; of state-wide phases of the program; of postgraduate medical education through refresher courses in obstetrics and pediatrics; of midwife supervision; of coordination of health-department activities in maternal and child health with those of medical, dental, and lay groups; and of continuous state-wide education programs in maternal and child health for the laity. Close integration of his work with the work of the other divisions of the state

health department is, of course, taken for granted.

Special consultation services by qualified specialists in obstetrics and pediatrics has been made available to local practitioners in a number of states. In several Southern states these consultants are employed full time; in other states the obstetrician or pediatrician in charge of postgraduate instruction gives, on request, consultation to local practitioners. Obstetric and pediatric postgraduate courses have been very greatly extended. Every Southern state has had some such program within the last 2 years.

Four Southern states and the District of Columbia have nutritionists. Specialists in health education are being added to the staffs.

In public health nursing, special consultants in maternity nursing have been added or plans to add them are being made in a number of states. One of the most interesting projects has been the use of nurse-midwives for the instruction of midwives. In two Southern states instruction is carried on not only by ordinary classes and home visits but also by actual bedside instruction at the time of delivery. In two states nurse-midwives are actually delivering a certain number of indigent patients at the request of the local physicians in certain small areas where physicians are few (in one state this is service under private auspices). Nursing service at delivery as part of a general health service is being developed in a number of states, and plans are under way in several more.

The use of private physicians in prenatal, postnatal, and child-health conferences has been greatly increased, and frequently these physicians are paid an honorarium on the basis of the number of clinics held or the hours of service provided. Locally the conferences are administered by the director of the local health unit. Special consultation and assistance in the establishment of technics, particularly when the clinics are beginning, is furnished in a number of states by specialists in obstetrics and pediatrics under the general direction of the director of the division of maternal and child health of the state department of health.

In a few states considerable attention has been paid to programs for better care of premature and newborn infants, both in the home and in the hospital. Standards are being developed and enforced in maternity-home supervision in a number of states, either as a direct activity of the state department of health, or through cooperative arrangement with the state department charged with this duty.

Dental health programs have been greatly extended, and emphasis has been placed on research, education, and examination, and on corrective work.

The increased use of advisory committees with medical and lay representation is noteworthy.

In the crippled children's service also, the most striking development in the last 2 years has been the very great extension of service. As in the case of the maternal and child-health programs, this extension has been made possible not only by the Federal funds allotted for crippled children's services and by the state and local money that has been appropriated for matching these Federal funds but also by other funds from Federal, state, and local sources used in supplying additional personnel for general health and welfare purposes. This has enabled these groups to make greater contributions than formerly in case-finding and in after-care services for crippled children, which has in turn made possible better coordination of effort between health and welfare agencies and agencies in charge of the services for crippled children.

The greatest development has, of course, been in the work of the official agencies for services for crippled children. Before the passage of the Social Security Act seven Southern states (Florida, Kansas, Kentucky, North Carolina, Oklahoma, Texas, and West Virginia) had state-wide programs for the care of crippled children, and seven others had less extensive programs. Now Louisiana and Georgia are the only Southern states that do not have programs in operation. By the way, Oregon is the only state outside the South that does not have a program.

Programs for the care of crippled children have been established not only in a greater number of states but also in more complete form than before the passage of the Social Security Act. More children, especially from the poorer counties, are being treated. More complete care, and hence more efficient and more economical care, is being given to individual children.

Earlier case finding means more effective treatment. If the crippled children's agency had sufficient funds so that it need have no waiting list; if local health services were organized and

operating in all parts of each state; if the maternal and child-health and communicable-disease work in these local services were given adequate attention, both by health-department personnel and by practicing physicians—then the problem of early case finding would be solved—assuming, of course, effective coordination between agencies. But, although this millennium has not yet been attained, progress is being made through such devices as the reporting, on birth certificates, of congenital defects and birth injuries, the furnishing of the crippled children's agency with epidemiological reports of diseases such as poliomyelitis—in brief, through better coordination between the health department and the crippled children's agency. The more extensive use of orthopedic diagnostic clinics at strategic points throughout a state and the interesting of medical and lay groups as well as the general public in the program also lead to earlier case finding.

The Southern states apparently agree that efficiency and economy in services for crippled children demand not only early care but also continuous and prolonged supervision; not only the provision of medical and surgical treatment but also of medical social service to assist the child and his family, when necessary, to make the social and psychological adjustments that the crippling may require; and in addition that vocational education should be provided so that the child may earn a livelihood. Developments along these lines have consisted of the provision of more adequate convalescent and foster-home care in order that a child might remain longer near treatment centers; the use of regional clinics as centers for periodic orthopedic supervision and treatment after discharge from the hospital as well as for diagnosis; the provision of physiotherapy in the child's own home; the use of public health nurses with special orthopedic training for assisting with the supervision of the child after his discharge from the hospital. Several state agencies are building a staff of public health nurses with special training in orthopedic nursing who will eventually act as special consultants to the local public health nurses who will have the immediate nursing supervision of the crippled child. The medical social workers have a similar relation to the local welfare personnel, besides giving consultation to other staff members and handling cases presenting especially difficult medical-social problems. The use of convalescent homes and boarding homes has also been found to make earlier care possible for many children by freeing hospital beds for other children.

In many states registers are being completed so that they will include every crippled child in the state.

More definite and higher standards for hospitals, convalescent and boarding homes, and for personnel are being formulated. A number of states have made eligibility for certification by the American Board of Orthopedic Surgery a requirement for orthopedic surgeons, and are using standards for other workers which have been set up by their national professional organizations.

Where it has been impossible to obtain staff members meeting these qualifications—for example, in physiotherapy, in orthopedic public health nursing, or in medical-social work—leave and scholarships have been furnished in a number of cases to staff members sufficiently well qualified to warrant further training.

During the past year, in several instances, administrative responsibility for services to crippled children has been transferred to the state health department. There is also a trend toward the employment of physicians as medical directors and as administrators. Where the program is not directed by a physician—and even where it is—medical technical advisory committees are giving more and more assistance.

Increased cooperation with agencies and groups working in related fields is also evident. This has been accomplished not only by the use of advisory committees and by formal agreements between agencies but also by the working out of definite technics of referrals.

The poliomyelitis epidemics in several Southern states have focussed attention on the need for services that will prevent the crippling of the stricken children and have brought about considerable increase in services to the child in his own home.

Both in the maternal and child-health and in crippled children's programs the Southern states provide an interesting diversity of local problems. There are even more striking differences in approach to similar general problems and in the selection of problems for attack. The two programs provide interesting contrasts, because in one the element of education and in the other

the element of medical care has been most emphasized. In each program we are learning things that can apply to the other.

As well-established technics are being extended, with resulting increase of efficiency in certain phases of the maternal and child-health and crippled children's programs, it is becoming more and more possible to try out new technics and to attempt the solution of the many problems in both fields that had not heretofore even been touched.

DISCUSSION (*Abstract*)

Dr. J. J. Repa, Montgomery, Ala.—I would like to relate the work that we have done in Alabama in maternal and child hygiene.

Appreciating the need for better care of infants, particularly under one month of age, in order to bring about a reduction of natal deaths, a full-time pediatrician was employed in May, 1936, to direct a Division of Child Hygiene associated with our Bureau of Hygiene and Nursing following the recommendation by the State Board of Health. The duties of the pediatrician as outlined are to establish refresher courses in pediatrics throughout the various counties of the State, read papers and give talks on this subject to medical groups as well as pertinent talks on child-health to civic and lay groups. At the end of 1936 it was our observation that more educational work could be accomplished by means of so-called pediatric group conferences in which several interesting pediatric cases were presented to a small group of physicians in the form of a clinic in which each physician could question the patient's parents, make an examination of the patient and, following the dismissal of the patient, join in the general round discussion. This program is designed to refresh the general practicing physicians in the general care and handling of babies. Some of the many topics discussed in these conferences are: care and disorders of the new born, prematurity, congenital syphilis, infant feeding, communicable diseases, childhood type tuberculosis, and colitis.

While other phases of the program are continued as usual, the pediatric group conference has proven to be the most successful plan of arousing the interest of the physician in the better care of babies.

A Negro pediatrician was added to our staff on July 1, 1937, having been loaned to us by the Children's Bureau to carry on a program among the Negro physicians in the State similar to that offered to the white physicians. He will remain with the department for a period of one year.

Two new divisions have been created during the past year: the division of oral hygiene with a dentist in charge, and the division of maternal hygiene under the supervision of an obstetrician.

The personnel of the division of oral hygiene, consisting of the dentist and an oral hygiene teacher, promotes an educational program largely through the schools, lecturing at meetings of teachers and in the school room, and in addition contacting the local dentists for promoting their interest in correction of dental defects and oral hygiene education.

In the division of maternal hygiene the obstetrician has associated with her a nurse-midwife who has been employed by the State for some time and two recently added obstetrical nurses. The duties of the obstetrician will be largely educational for physicians and midwives. She will supervise the prenatal clinics and instruct physicians who are in attendance, lecture to county medical societies, put on demonstrations and show educational motion pictures. In addition, she will have charge of the midwife control program, having under her supervision the nurse-midwife, who in turn visits the counties as a field advisory nurse and aids the county health nurses to formulate an adequate midwife program.

The two obstetrical nurses included in the division will be placed in Cullman County to determine the practicability of the utilization of their services in assisting physicians at home deliveries. It is anticipated that these nurses will have time to make postpartum visits and assist in prenatal clinics. Experience gained in Cullman County will be used to determine the scope of activities that may be expected in this particular field. It will be used also as a basis for recommending the employment of obstetrical nurses in other areas.

Dr. John M. Saunders, Nashville, Tenn.—The maternal and child-health program in Tennessee has been increased by funds from the Social Security Bill. Since the best way to reach mothers and children is through local health departments, maternal and child-health programs of local communities have been strengthened and increased.

Effort is being made to have as many expectant mothers as possible under medical and nursing supervision. Special attention is given to the education of expectant mothers who do not already know the value of medical and nursing supervision, for this is the group which is mainly responsible for the high maternal and infant death rates. Maternity classes have been organized in some areas so that the nurse may extend her teaching to a larger number of antepartum cases. The drawing of blood for a Wassermann test on all antepartum cases under medical and nursing supervision is rapidly becoming a routine procedure and antisyphilitic treatment given whenever necessary.

Midwifery is a problem of paramount importance. Midwife classes are being conducted on a planned schedule and systematic home visiting of midwives is being done for the purpose of teaching midwives the fundamentals of cleanliness and the importance of calling on a physician in abnormal cases.

For the past year a postgraduate course in obstetrics, which is sponsored and financed by the Tennessee Medical Association, the Commonwealth Fund, the State Department of Public Health, Vanderbilt and the University of Tennessee Medical Schools, has been conducted. This program will continue for another year so that every physician in the State will have the opportunity of attending the course.

Since the high death rate among infants under one month of age is due, to a large extent, to deaths among premature infants, the infant program of the Tennessee Department of Public Health has inaugurated measures for combating mortality in premature infants. This program for premature infants has of necessity been directed towards the better care of small infants in

homes because only 19 per cent of all live births occur in hospitals.

The real extent of the premature problem in Tennessee is not known because this item is not always filled out on the birth certificate, but it is believed that the incidence is more than 2 per cent as reported for all births for the years 1934-1936. An effort is being made to have all physicians and nurses know the problem associated with premature births and as much as possible about the care of these infants.

In order to bring the problem of premature births closer to the attention of local health officers the summary birth card used in local health departments has been revised to include a statement of whether the birth was full-term or premature. It is expected that this procedure will enable the local health officer better to realize the extent to which premature births influence infant mortality in his local community. Also, it is expected that better reporting of the period of gestation of a birth will result when emphasis is placed on this factor. Then a truer picture of the incidence of prematurity should result, especially in areas where the reporting of births is good.

If private physicians are shown methods which they can use in their private practice, it is believed that greater interest will be shown by them in the care of premature and small infants. For this reason, a simple, inexpensive box for premature infants is demonstrated to physicians. Local health departments are securing these beds for loan to private physicians whenever they desire to use one for a premature infant which they have in their private practice.

The box, which has been adapted from one described by Mott in *Modern Hospital* (Vol. 41, page 100, December, 1933) is made of wood. It is heated by electric light bulbs which are placed under a false bottom. If the box is to be used where electric current is not available, it may be heated by bottles of hot water or by warm bricks placed under the false bottom. The box is a combined bed and heating chamber. It is easy to construct and may be made for a cost of about $4.00.

Because the preschool period is an important one, effort is being made to reach more children under school age through child-health conferences. Continuous medical service is important and for this reason permanent child-health conferences have already been established in some areas in the State.

It is important that analyses of maternal and child-health problems be made so that one will have a better understanding of actual conditions as well as for the purpose of guiding the program. Already local health departments are carrying on maternal and infant mortality studies, and studies of these problems on a State-wide basis are being made. Effort is being made to acquaint all local communities with their maternal and infant problems through mortality and morbidity analyses.

Dr. R. C. Hood, Washington, D. C.—I want to emphasize the importance of safeguarding the quality of care provided under this program. Second, I want to point out the desirability for the integration and utilization of the services of public, private, and lay groups in this field. Third, I want to point out the necessity for the development of this program on a state-wide basis. And finally, I want to urge that recognition be given to the need for a broad program of services extending beyond mere physical restoration and leading to economic and social adjustment.

VARICOSE VEINS OF THE BROAD LIGAMENT AND THEIR CONSEQUENCES*

By PETER B. SALATICH, M.D.
New Orleans, Louisiana

In the routine examination of cases of low backache in women, the pelvic organs are often thought of as the probable cause, especially if a history of menstrual disturbances is given.

In the year 1907, while working in the clinics and also in private practice, I observed many marked retrodisplaced uteruses attended with practically no pain nor menstrual disturbance, while other women with displaced wombs suffered greatly and gave histories of marked menstrual disturbance. It occurred to me that displacement alone was not the cause of these disturbances. Therefore, I decided to study these cases before, during and after operation.

Invariably, those who complained most had more or less enlarged veins in the broad ligaments and a simple shortening of the round ligaments did not relieve them. In studying my own cases and also those operated upon by other men at the hospital, I found that simple suspension relieved them for a while, but in a large percentage of cases the backache returned.

It then occurred to me that mere suspension was not relieving the dilated veins, which at the time were given little thought as a cause of backache. I had occasion to operate again upon my own cases and those of others, and found the veins just as prominent as they had been before the uterus was suspended. At the second operation, when it was possible, the veins, especially the ovarians, were ligated, and shortening of the utero-sacral ligaments relieved the deeper and more inaccessible ones around the uterine arteries.

Emge describes five plexuses of veins in the pelvis with which we are concerned:

"The vaginal, uterine, and hemorrhoidal plexuses, which drain into the inferior hypogastric vein, and the pampiniform plexuses which empty through the ovarian veins into the vena cava on the right and the renal vein on the left. In this venous structure there is only one valve which lies at the end of the right ovarian vein."

Dudley says:

"The causes [of varicose veins] are either constitutional or mechanical. The veins on the left are more

*Read in General Clinical Session, Southern Medical Association, Thirty-First Annual Meeting, New Orleans, Louisiana, November 30--December 1-2-3, 1937.

*From the Postgraduate Department of Gynecology of the School of Medicine of Louisiana State University, New Orleans.

prone to be varicosed than those on the right, because those on the left have a long course emptying into the renal, while those on the right empty into the inferior vena cava and have valves."

This explanation may be adequate for the ovarian veins, but the uterine veins seem to be just as prone to dilate on the right as on the left. These are the veins that I believe cause most of the symptoms of backache.

Mattson divides the etiological factors into predisposing and active:

"The predisposing causes are: first, the anatomic peculiarities of the venous system; second, visceroptosis; and third, poor general health with impaired muscular tonus. Among active causes, pregnancy with subinvolution and pelvic engorgement is given the most prominent place. Other causes are: retroversion, pelvic tumors, obstipation, excessive sexual intercourse, particularly when not satisfied."

Emge concludes that varicose veins are due in the large majority of cases to damage of the fibro-elastic suspensorium, and that conservative measures are usually sufficient to cure the condition.

Symptoms.—Pain is one of the principle complaints. Crosthwait refers to this pain as very characteristic. It is affected by the position of the patient, sometimes being intolerable when the patient is on her feet. A patient suffering from well developed varicosities of the broad ligament will often become a chronic bed-ridden invalid.

Tracy writes:

"The patient complains of weight and discomfort or a dull pain in one or both sides of the pelvis, is usually indisposed, tires easily, and suffers from backache. There is usually leukorrhea and there may be dysmenorrhea. As a rule the bowels are constipated."

In young subjects menstruation may be very profuse, gradually lessening and often coming on twice a month. According to Pigford, at times there is also an increase in the menstrual cycle, menstruation being at shorter intervals. At first, there is ovarian congestion, causing over stimulation, with resulting hyperplasia of the endometrium and fibrosis, preventing the development of the graafian follicles, and interfering with the blood supply. The flow ultimately becomes irregular and scanty. Quite often there is leukorrhea of the hydrorrhea type.

A careful history and thorough pelvic examination to eliminate varicose veins as the cause of the profuse menstruation should be made before radium is used. The bleeding may be checked, but the veins, which are composed of rather thin coats, may be subjected to greater danger of rupture than before. Hirst reports a case of rupture of the varicose veins in the broad ligament of a woman who, during the time of menstruation, attempted to carry a heavy coal scuttle up a flight of stairs, but on the way was seized with violent pains in the abdomen and fainted. Radium will check the menstrual flow, but has very little effect on the backache associated with these cases, whereas a conservative operation would relieve both conditions.

With a history of disturbances in the menstrual flow, lessening when lying down, increasing when about; pain in the lower back, always worse when walking, and often going down the thighs, relieved upon lying down, a probable diagnosis of varicose veins as the cause of the trouble may be made. Opinion is divided as to the merits of rectal examination as a means of diagnosing this condition. Some claim that bimanual examination in the standing position or recto-abdominal palpation will often reveal a doughy, beady mass in the broad ligament, which will become much smaller when the patient is placed in the recumbent position, and the ligament will be felt thickened. In thin patients this differentiation is easier to carry out. Other men claim that they are not able to find this condition after careful trial of the method.

My experience has been that the uterus need not be retroverted in cases of varicose veins. I have found the following method helpful in making a diagnosis:

The fingers are passed to the sides of the cervix, keeping in line with the axis of the uterus, pressing upward in the parametrium. If enlarged veins are present this will cause considerable pain. Generally the cervix is softer than normal and the body of the uterus boggy in feel. To eliminate the possibility that ovaries or tubes are the cause, the finger is directed anteriorly and upward. If the tube and ovary, when palpated, are found not enlarged nor painful, we should look to the veins as the cause of the trouble.

Conservative operation is generally sufficient to relieve these cases. The technic of operation which I prefer is as follows:

When the abdomen is opened and the field of operation is visualized, we generally see the uterus, the fundus back in the *cul-de-sac*. It resembles an old piece of dough, the color greyish, the capillaries of the pelvic organs and perito-

neum increased and dilated. Lifting the uterus, we see the body enlarged, irregular in shape, mottled in appearance, and softer than normal. The ligaments are loose, allowing the uterus to be pushed in any direction. The tubes are often congested. The ovaries generally contain cysts, the size depending upon the chronicity of the case. Either they are not large enough to need attention or they have destroyed one or both of the ovaries. Examination of the broad ligament shows a generalized enlargement of both the ovarian and the uterine veins on one or both sides. Often we notice a marked enlarged and tortuous condition of the veins about the uterine arteries. I believe they are more responsible for the backache complained of than are the dilated ovarians.

The next step is to locate the uterosacral ligament. This is often difficult. Remembering that they are attached to the uterus about the line of the internal os, by drawing the uterus upward and to one side they will be seen. They are clamped and by traction in a downward direction the fold of the peritoneum leading to the promontory of the sacrum is seen. This fold is plicated with linen thread and the ends are left untied. When they are placed, by traction on both we can tell whether they have been sufficiently shortened. A space large enough to insert three fingers into the *cul-de-sac* is generally sufficient. The round ligament should also be shortened. I prefer the Ohlausen's method. Inspection before closing the abdomen will show the uterus well supported, diminished in size; the boggy, mottled and irregular appearance has given way to a pinkish white color and the uterus is firmer and regular in outline.

SUMMARY AND CONCLUSIONS

(1) Patients who complain of back pain, especially that relieved by resting and associated with menstrual disturbance, should be studied for possible varicose veins in the broad ligament.

(2) Ovaries containing small cysts in these cases need not be disturbed. The correction of the varicosity will relieve disturbances by improving the blood supply.

(3) Radium should be used with caution in varicocele cases.

(4) Retrodisplacement is not always found in cases of varicosities.

(5) Marked leukorrhea may be kept up by the passive congestion occasioned by varicosity of the veins in the broad ligament.

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M. Y. DABNEY, M.D., Editor
EUGENIA B. DABNEY, M.S., Associate Editor
C. P. LORANZ, Secretary, Treasurer and General Manager

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EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
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UTERINE ADENOMA

Experimental malignant growths have been produced in various animals by continued irritation, by feeding a commercial vitamin E rich material, and by inoculation. Recently, tumors of the uterus have been accidentally discovered in an animal laboratory which in etiology and course bear a closer resemblance to those of human beings than any experimental growths so far reported.

In a colony of five hundred female rabbits observed over the last four years at Princeton, New Jersey,[1] eighty-three "spontaneous" or accidental tumors of the uterus were detected. Many were diagnosed during the animal's life, successfully transplanted, and symptoms studied during the growth of the original tumor and the transplant.

The tumors could be diagnosed by palpation if they were large. The reproductive activity of the rabbits was routinely recorded and disturbances of reproductive function always occurred four to five months before the tumor could be detected. Fertility was diminished. One-third of the animals became suddenly entirely sterile. Others delivered dead fetuses. Retention of fetuses past term, abdominal pregnancies, toxemia of pregnancy, abortion and other abnormalities were encountered. In one-fourth of the cases of uterine tumor, cystic breast changes occurred, which resembled chronic cystic disease of women.

All the tumor-bearing animals were two years or more old; nearly half were in the fourth year. Certain breeds of rabbit were particularly susceptible.

The pathology of all the growths was the same. Small nodular thickenings of the endometrium were frequently noted at autopsy. Early tumors were pedunculated. Tumors which were palpable in life had usually invaded the muscle. The surfaces of the older growths were ulcerated and metastases were associated with extreme necrosis. The thyroids and suprarenals of the tumor-bearing animals showed frequent abnormalities. The changes in suprarenal tissue resembled those detected in the same rabbit colony in toxemia of pregnancy, and also those in other groups of mice and rabbits after treatment with the estrogenic hormone. No explanation of the cause of the growths is offered by the investigators, though it is concluded that a dietary toxin was not responsible.

One would think that the etiology might be related to the laboratory diet, close confinement in quarters at rather constant temperature, lack of exercise, and protection from exertion or violent death which permitted ailing and defective animals to live on into the cancer age. All these factors are likewise associated with the development of human cancer, and for this reason are of particular clinical and gynecologic interest.

1. Greene, H. S. N.; and Saxton, J. A.: Uterine Adenomata in the Rabbit. Jour. Exper. Med., **67**:691 (May) 1938.

LICE AS A DEFICIENCY DISEASE

In 1910, Funk's original anti-beriberi food factor was studied intensively. In the last decade Funk's concentrate has been subdivided into so many different components that physicians may well feel discouraged and abandon hope of clinical and dietary placing of the B vitamins, which now number six.

The medical practitioner may now be almost in the position of the Negro waiter in a restaurant who was called excitedly and indignantly to his table by a patron.

"Look here," raged the customer. "This is a filthy lunch room. There is a bug in my soup."

"Naw, sir, boss," soothed the darkey. "Dat

ain't no real insec'. You look at it close. You can see dat ain't no bug at all. Dat's one er dem vitamin bees."

It is some aid to the practitioner to recall that the B vitamins are all water-soluble but not closely associated with the water-soluble antiscorbutic C. They are physiologically and chemically different from C, and they are not abundant in citrous fruits. Several crystalline chemicals have been separated from what was formerly called vitamin G, or B_2, and these have been shown to control different and distinct animal deficiency diseases. One of the B_2's is identified as nicotinic acid, apparently a specific for blacktongue and pellagra.

One of the several subdivisions of the former B_2 is riboflavin. Without riboflavin, rats are stunted in growth, frequently lose fur and have yellow scales on their skin. Gyorgy,[1] of Western Reserve University, after studying several thousand rats on different types of B-deficient rations, observed that about a hundred and twenty of the six hundred riboflavin deficient were infested with lice, while pediculosis was not detected in any of the other groups on rations deficient in the various other components of the B-complex. When riboflavin was administered by mouth, the lice disappeared, the animals' fur grew normally again, and general body growth was resumed.

It is a somewhat novel idea that the bite of a many-celled animal on the skin may be prevented by proper feeding, or by any kind of internal medication.

Bacterial diseases such as syphilis and gonorrhea are treated by internal antiseptics. Larger, many-celled organisms such as lice outside the body, are usually protected by the skin itself from substances within the blood. The disappearance of lice after adequate feeding of the host suggests something like an antibody action. It is entirely unlike the direct destructive effect of an externally applied antiseptic on the louse. Among human beings, though pediculosis is usually a disease of the poor, associated with filth, the well-nourished contact is almost instantly infested after any kind of exposure. Chickens and hogs raised for the market, even those under the best conditions, are regularly "deloused," or treated for lice with external antiseptics. An internal treatment for pediculosis would be a boon to physicians, soldiers, and animal husbandry.

In the diseases accepted as dietary deficiencies, not twenty, but usually a larger, per cent of the animals develop symptoms. If the above work is repeated, and it is shown that a fifth of the animals on a riboflavin-free diet in other laboratories regularly develop pediculosis, then further analysis would be in order of the blood factors which predispose to pediculosis. One would expect deficiency of vitamin A, D, E or almost any other deficiency to lower resistance. It is a source of surprise that animals with deficiency of the various other components of the B complex showed no lice. There have been many instances of disappearance of a specific infection in the malnourished after proper feeding.

Evidence that pediculosis is curable by feeding is outweighed by evidence that it is a highly contagious infestation which has no immunes. The work reported, however, on cure of pediculosis by administration of riboflavin deals with a large number of animals under apparently well controlled experimental conditions.

1. Gyorgy, Paul: Pediculosis in Rats Kept on a Riboflavin-Deficient Diet. Proc. Soc. Exper. Biol. & Med., **38**:383 (April) 1938.

GLEANINGS FROM RECENT JOURNALS

Poisoning with Heavy Metals.—Radium, lead and calcium have many reactions in common in the human body, one great difference being of course that the first two are highly toxic, while the latter is an essential building material for the living animal, also capable of course of toxic effects.

Both radium and lead tend to be deposited in bone, the site also of calcium concentration. Radium poisoning has been treated by injections of parathyroid hormone, which stimulates excretion of any of the above metals in the body. By mobilizing calcium and raising its level in the blood, parathormone may cause disintegration of bone.

Symptoms of lead poisoning are made worse in the summer, according to Brooklyn investigators,[1] by the action of ultraviolet light, which raises the level of both calcium and lead in the blood and bones. Vitamin D has the same effect.

It has been suggested elsewhere[2] that porphyrinuria is a concomitant of lead poisoning. Por-

1. Sobel, A. E.; Gawron, O.; and Kramer, B.: Influence of Vitamin D in Experimental Lead Poisoning. Proc. Soc. Exper. Biol. & Med., **38**:433 (April) 1938.

2. Gross, S. S.; Sasaki, Y.; and Spies, T. D.: Effect of Nicotinic Acid on Increased Porphyrinuria Occurring in Seven Painters. Ibid, p. 289. Editorial: Liver and Porphyrins. Sou. Med. Jour., **31**:574 (May) 1938.

phyrin is a photosensitizing agent, presumably an indicator of liver injury, and its presence in the body has been offered as explanation of the sensitivity of pellagrins to sunlight. Possibly both pellagrins and persons suffering from lead poisoning are made sensitive to sunlight by the same mechanism, in which porphyrin metabolism is important. One would then expect vitamin D to make pellagra worse, just as sunlight does, perhaps to increase the porphyrinuria of pellagrins; and one might estimate porphyrinuria as a possible indicator of recovery from lead poisoning. These metabolic studies show an increasing clinical significance.

It has been suggested that nicotinic acid, which is dramatically beneficial in pellagra, may likewise alleviate some of the symptoms of lead poisoning.

Toxemia of Pregnancy.—Toxemia of pregnancy is difficult to reproduce in animals. However, Greene,[1] of the Rockefeller Institute at Princeton, has observed outbreaks, almost epidemic in proportion, in rabbit colonies, which present analogies with the human disease. The majority of the animals were overfat. Convulsions were noted, acidosis, air hunger, dyspnea and considerable thirst. The rabbits were frequently found dead with their heads in the water containers. Both hypo- and hyperglycemia were detected. At autopsy, characteristic lesions of the adrenals were observed as well as of the liver and kidneys.

The rabbit thirst suggests a disturbance of water metabolism, which Strauss,[2] of Harvard, considers an important feature of the same disorder in human beings. Only women who gain weight excessively during gestation develop true toxemia, according to Strauss. The weight gain he considers a sign of abnormal water retention which in turn is due to dietary deficiency, chiefly to protein deficiency. There is an increased requirement for various food elements in gestation and lactation, in particular for protein and for vitamin B_1, and a deficiency of these may result in abnormal water retention in the tissues. In pregnant women with edema, the administration of considerable amounts of protein, liver and vitamin B_1 concentrates resulted in striking loss of weight.

The plasma protein level would seem a good indicator of impending danger, since a fall in plasma protein is apt to be associated with water retention. A group of women in the last trimester of pregnancy were observed by Strauss, with low plasma protein, increased water retention as shown by increased weight, and rise in arterial pressure. In these, the administration of sodium salts exaggerated the symptoms, increasing the albuminuria and often precipitating headaches, vomiting, visual disturbances and vertigo. Salt administration Strauss believes to be contraindicated in toxemia. Sodium should be avoided in the form of table salt, saline injections, or bicarbonate. For women with threatened toxemia he recommends increased protein, in particular. Vitamin B_1 and liver were also used with advantage.

It is unfortunate that occasional physicians still attempt to prevent weight gain in pregnancy by dietary restrictions, when the real need is for larger quantities of several essential food elements. The old idea that protein damages the kidneys and is dangerous in albuminuria also dies hard.

1. Greene, H. S. N.: Toxemia of Pregnancy in the Rabbit. Jour. Exper. Med., **65**:809, 1937; **67**:369 (March) 1938.

2. Strauss, M. B.: Observations on Etiology of Pregnancy. Production of Acute Exacerbation of Toxemia by Sodium Salts in Pregnant Women with Hypoproteinemia. Amer. Jour. Med. Sci., **194**:772, 1937; **195**:516 (April) 1938.

TWENTY-FIVE YEARS AGO

From Journals of 1913

Socialization of Medicine in England.[1]—"The crisis in the profession due to the national insurance act has at last arrived. As anticipated in my last letter, the representative meeting of the British Medical Association has declined the final offer of the government and launched what may be called a declaration of war against the scheme. As befitted such a momentous occasion, the debate was prolonged and animated. On the one side, it was maintained that if the profession held together it could win its terms, while if it did not it would be ruined. Many of the reasonable demands of the profession, such as payment for mileage, had not been met. No provision had been made for anesthetist's fee, though the physician was bound to perform minor operations. * * * At present there were certain areas of low-class practice in the country and no matter how bad were the terms offered by the government they were much superior to those under which physicians were working. * * *

"The fission described continues to increase and the profession is divided into two hostile camps, denouncing one another. * * * Those who have agreed to work the act are denounced as 'traitors,' 'pledge breakers.' * * * Placards in the streets bear evidence of the struggle. * * * 'Choose your own doctor' * * * and on the other side, 'Collapse of the doctors' strike.' * * * The ill feeling between the two sections of the profession is so great that many old friendships will be severed."

Bills before the State Legislatures.[2]—In Kansas, "S.B.

1. Medical News. London Letter. J.A.M.A., **60**:219, 1913.

2. Medical Economics. J.A.M.A., **60**:467, 1913.

76, reorganizing the State Board of Health and providing for four physicians, four business men and one lawyer on the board, has been defeated in the House. S.B. 248 reorganizes the board and provides for a board of four physicians, one registered pharmacist, one manufacturer, one person engaged in the wholesale business, one person in the retail business and one farmer. These bills are said to be introduced in the interest of the packing interest of the State who wish to put a stop to the activities of the present board in the prevention of food adulteration."

In Minnesota, "The State Board of Health has asked for an appropriation of $45,000 for a district health officer in each congressional district. A bill has been introduced abolishing public drinking cups, also one amending the present cold-storage bill; also a bill requiring all persons engaged in the manufacture, handling or sale of any foodstuffs to secure a certificate showing that they are in good health."

In California, "a number of bills affecting public health have been introduced, including a bill to abolish compulsory vaccination; a bill to require reports on occupational diseases; a bill to reorganize the State Board of Medical Examiners and to create three boards of nine members each: one board of medical examiners of physicians, including three homeopaths and two eclectics; one board of examiners of drugless healers, composed of two osteopaths, two chiropractors, two mechanotherapists, two naturopaths and one 'metaphysician,' and one board of 'religious practitioners' composed of nine members, no more than three of whom shall be members of any one system. Evidently religious systems are plentiful in California."

Oklahoma City — Where We Meet

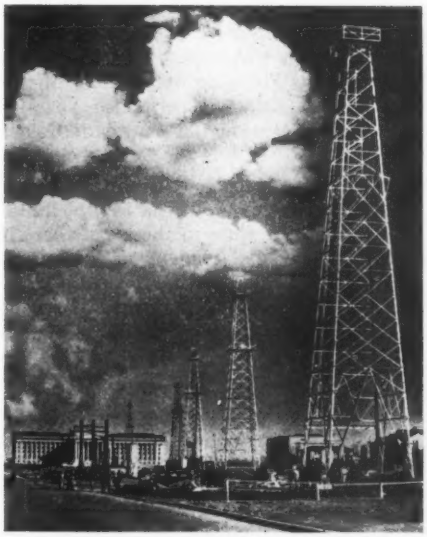
THE CAPITAL CITY*

In earlier chapters of the story of "Oklahoma City, Where We Meet," reference has been made to thrills and romance in the history of the still young state, to the "Run" that opened the "Oklahoma Country" to white settlement in 1889, to the bringing in of oil gushers in fine residential district backyards, etc. The present chapter has to do with an incident of Oklahoma history without precedent, that can have no parallel anywhere, the removal of the state capitol from Guthrie to Oklahoma City literally "between two days."

It was definitely understood in 1906 that Oklahoma would enter the Union as a Democratic state, and the Oklahoma Enabling Act, passed that year by Congress, which was Republican, undertook to protect the republican city of Guthrie as the state capital until the year 1913. The statehood proclamation was effective November 16, 1907. Charles N. Haskell, the new governor, a staunch Democrat, never acknowledged the legality of the capital clause of the Enabling Act, and began immediately to arrange for a statewide election on the capital location question. The election was held Saturday, June 11, 1910, with Guthrie, Oklahoma City and Shawnee as the three contenders.

Haskell went to Musgokee, his home, to vote. Late in the day he went to Tulsa to speak to the Chamber of Commerce. He had arranged previously to receive the returns, and when it became evident that Oklahoma City had won he ordered a special train to take him to Oklahoma City.

In the meantime he telephoned his secretary, W. B. Anthony, who had voted at Marlow, and instructed him to take the Seal of State to Oklahoma City immediately. Anthony called Bill Cross, Secretary of State, Earl Keys, an assistant, and Paul Nesbit, then chief clerk in the Governor's office, and arranged a meeting near the Logan County court house, in Guthrie, where the Governor's office had been located since statehood. Keys and Nesbit entered the building, telling the guard they were after a laundry bundle. They brought out the bundle, and in it



Oil wells on State Capitol grounds at Oklahoma City

*Prepared by the Publicity Department of the Oklahoma City Chamber of Commerce for the SOUTHERN MEDICAL JOURNAL.

the Great Seal of the State of Oklahoma. The ride to Oklahoma City was made by Anthony immediately in a car provided by the Oklahoma City Chamber of Commerce. He arrived at the Lee-Huckins Hotel in Oklahoma City at 4:00 a.m., Sunday, June 12. There he met Governor Haskell and they immediately hung a sign on the door of the Governor's room reading "Governor's Office," thus establishing Oklahoma City as the capital city.

Guthrie obtained a state supreme court decision that the election had had certain irregularities which nullified it, and for a time the capital was back at Guthrie, in a *"de jure"* sense but scarcely so *"de facto."* Within half an hour after the supreme court's decision was announced, Governor Haskell, going to Guthrie by train and signing the proclamation between trains in the Guthrie station of the Santa Fe railroad, called the legislature into extraordinary session at Oklahoma City, and returned immediately to the city the people had chosen as their capital.

Quarters for the legislative session were provided in an Oklahoma City office building, and the legislature, recognizing the election as a clear expression of the will of the people, soon passed a bill naming Oklahoma City as the capital of the state. A legal battle raged for several years, but the United States Supreme Court finally held that, with the statehood proclamation by President Roosevelt, Oklahoma had become a sovereign state in all respects equal to any and all other states of the Union, and that the attempted restriction of the Enabling Act in favor of Guthrie as the capital for a period of years was *"ultra vires"* or beyond the powers of Congress to impose.

In the election campaign, citizens of Oklahoma City had promised to provide a capitol building without cost to the state in the event that their city should win. They made good on the promise in a big way, deeding to the state a large number of tracts of land northeast of the city, which lands included scores of acres now among the richest of all Oklahoma oil lands. Upon these acres, those attending the Southern Medical Association meeting in Oklahoma City in November, will find a state capitol entirely surrounded by oil wells. These wells, irrespective of the surface value of the land, are yielding and for many years will continue to yield wealth far in excess of the cost of the state's fine capitol building, or several more like it.

Book Reviews

Management of the Sick Infant and Child. By Langley Porter, B.S., M.D., M.R.C.S., (Eng.), L.R.C.P. (Lond.), Dean, University of California Medical School and Professor of Medicine, and William E. Carter, M.D., Director, University of California Hospital Out-Patient Department. Fifth Revised Edition. 874 pages, illustrated. St. Louis: The C. V. Mosby Company, 1938. Cloth $10.00.

Six years have elapsed since the last edition of this book, this being the fifth edition. In that period of time many new drugs and methods of treatment applicable to infants and children have arisen. All of these newer methods have been included in this revision. The book is divided into three parts. The first part deals with the etiology and treatment of various symptoms, such as vomiting, diarrhea, fever and convulsions. Treatment is described in detail. In the second part the authors describe the symptoms and treatment of the diseases of the various systems of the body, including allergy, behavior problems and the acute infectious diseases. Part three is devoted to the therapeutic methods, which are given in great detail with excellent illustrations. Exact directions for the preparation of formulas and recipes are given. This is followed by a chapter devoted to drugs in which many prescriptions designed to alleviate symptoms are given. Taken as a whole, the book is well written and should prove of distinct value to physicians in general practice and to those specializing in the diseases of children.

A Primer for Diabetic Patients. By Russell M. Wilder, M.D., Ph.D., F.A.C.P., Professor and Chief of the Department of Medicine of the Mayo Foundation, University of Minnesota; Head of Section on General Metabolism, Division of Medicine, The Mayo Clinic. Sixth Edition, 191 pages. Philadelphia: W. B. Saunders Company, 1937. Cloth $1.75.

This little book is written primarily to teach the patient how to handle his diabetic condition. It explains what diabetes is. The usual tests for diabetes, the use of protamine insulin, treatment, complications, and diets are all well outlined. The calculation of diets, the weighing of foods, and food tables are all included. Although the book is not so complete as it might be, nevertheless it is a handy little volume that can easily be slipped into one's pocket. As a guide to the patient in the understanding and treatment of his disease, it serves a useful purpose.

Syphilis, Gonorrhea and the Public Health. By Nels A. Nelson, B.S., M.D., F.A.P.H.A., Director, Division of Genitoininfectious Diseases, the Massachusetts Department of Health, and Gladys L. Crain, R.N., Epidemiologist, Division of Genitoinfectious Diseases, the Massachusetts Department of Public Health. 359 pages. New York: The Macmillan Company, 1938. Cloth $3.00.

This excellent book on venereal diseases from a social and public health standpoint is easy to read and entertaining. It will be of great value to social workers, nurses, public health officials, physicians, and those of the laity who wish to become better informed on the subject of venereal diseases. It presents the essential

facts concerning these diseases, the medical as well as the public health problems. It is an excellent book to be read by those who remain so mid-victorian that they consider venereal diseases a moral issue and not a public health problem.

The portion of the book dealing with the diagnosis, pathology and the treatment of these diseases is not sufficiently advanced to be of value as a reference. It was not the author's intention to produce a monograph, but to present in an easily understood language the facts concerning these diseases.

The charts and statistics covering the instance, morbidity, and mortality of gonorrhea and syphilis will impress the reader with the magnitude of the public health problems the United States faces in venereal diseases. The programs to control their spread are of great interest.

The only criticism to be made of the book is that after reading it one is left with the impression that adequate treatment can be secured only from charity clinics or a specialist. Modern, scientific treatment is today being rendered to thousands of persons infected with venereal diseases by their family physician. This treatment is superior to that rendered in overcrowded charity and part-pay clinics.

"Syphilis, Gonorrhea and the Public Health" is especially recommended to those who wish to go into venereal diseases from a public health viewpoint. It is highly recommended to social workers, nurses, public health officials, physicians and those of the laity who wish to obtain accurate, modern and up-to-date information concerning these diseases.

Pneumonia and Serum Therapy. By Frederick T. Lord, M.D., Clinical Professor of Medicine, Emeritus, Harvard Medical School; Member of the Board of Consultation, Massachusetts General Hospital; and Member of Massachusetts Advisory Committee on Pneumonia, 1931-1935, and Roderick Heffron, M.D., Field Director, Pneumonia Study and Service, Massachusetts Department of Public Health, 1931-1935. Revised Edition of Lobar Pneumonia and Serum Therapy. 172 pages. New York: The Commonwealth Fund, 1938. Cloth $1.00.

This comprehensive little handbook summarizes present knowledge of serum treatment of pneumococcus pneumonia. Numerous references to other articles on the subject are given.

Among the things stressed in the book are (1) etiology of lobar and bronchopneumonia, (2) the clinical and laboratory diagnosis, (3) selection of cases for serum treatment, (4) precautions before the use of serum, (5) method of administration, (6) dosage, (7) types of reactions occurring after serum and the treatment of each of these, and (8) the results of treatment of pneumococcus pneumonia with antiserums.

The authors emphasize the importance of early diagnosis, typing the organism by the Neufeld method and the institution of serum therapy in the first three or four days of the illness.

It is suggested that larger than the average dose of serum be given in each of the following situations: (1) when the patient is more than 40 years of age, (2) when a bacteriemia is present, (3) during pregnancy and the first week of the puerperium, (4) when the infection is spreading or when more than one lobe is involved, and (5) when serum therapy is begun after the fourth day of the illness.

Tables showing the mortality rate in treated and untreated cases are convincing as to the value of serum for Types I and II. The number of cases treated with serums against the higher types is too small to allow any definite conclusions to be drawn.

The use of rabbit antiserum is discussed, but since only a comparatively small series of cases has been treated no conclusions are drawn. However, it is felt that rabbit serum may have certain advantages over horse serum.

Concentrated horse serums against Types I, II, V, VII and VIII are now being used. Serums against certain of the higher types are being manufactured. Serums against Types I and II have been standardized as to potency, but serums against the higher types have not as yet been standardized.

Fever Therapy Abstracts and Discussions of Papers Presented at the First International Conference on Fever Therapy. College of Physicians and Surgeons, Columbia University, New York City, March 29, 30, 31, 1937. Edited by Members of the American Committee: Dr. Walter M. Simpson, Dayton, Ohio, Chairman; Dr. William Bierman, New York City, Secretary; Dr. Charles M. Carpenter, Rochester, New York; Dr. Charles A. Doan, Columbus, Ohio; Dr. Frank W. Hartman, Detroit, Michigan; Dr. Leland E. Hinsie, New York City; Dr. Frank H. Krusen, Rochester, Minnesota; Dr. Clarence A. Neymann, Chicago; Dr. Stafford L. Warren, Rochester, New York. 486 pages. New York: Paul B. Hoeber, Inc., 1938. Cloth $5.00.

This book deals with the reports made at the First International Conference on Fever Therapy. The first articles deal with biological and chemical aspects of artificial fever. A series of articles by authors from different countries are concerned with this method of treatment of rheumatic fever and chorea. The various writers seem to be in agreement that fever therapy has a dramatic beneficial effect in this disease. As regards its effect on rheumatic fever the opinions expressed lead to no definite conclusions. Some authors believe that artificial fever is beneficial in certain types of tuberculosis.

The next section of the book is concerned with the treatment of syphilis and of gonococcic infections. The reports indicate that not only late syphilis of the central nervous system, but also early syphilis may be markedly benefited, while further evidence of the therapeutic value of hyperpyrexia in infections due to the gonococcus is presented. The middle third of the book consists of the previous articles rendered in French and the last third of the book consists of the translation into German of the preceding reports.

The volume covers a highly specialized field in therapeutics, but is invaluable to anyone who is using this new and promising method of therapy.

BOOK REVIEWS contiuued on page 707

OFFICERS 1937-1938

The following is a complete roster of the officers of the Southern Medical Association for 1937-1938, of associations meeting conjointly with the Southern Medical Association and of the Oklahoma County Medical Society.

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American Society of Tropical Medicine (meeting conjointly with Southern Medical Association)—Dr. Mark F. Boyd, President, Tallahassee, Florida; Dr. Alfred C. Reed, President-Elect, San Francisco, California; Dr. Asa C. Chandler, Vice-President, Houston, Texas; Dr. Charles F. Craig, Editor, New Orleans, Louisiana; Dr. E. Harold Hinman, Secretary-Treasurer, Wilson Dam, Alabama.

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OKLAHOMA COUNTY MEDICAL SOCIETY, host to the Southern Medical Association, Thirty-Second Annual Meeting, November 15-18, 1938.

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Entertainment—Dr. Rex Bolend, Chairman; Dr. Gerald Rogers and Dr. D. W. Branham.

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Information—Dr. W. Floyd Keller, Chairman; Dr. G. E. Stanbro and Dr. C. R. Rountree.

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Women Physicians—Dr. Leila E. Andrews, Chairman; Dr. Mary V. S. Sheppard and Dr. Eva Wells.

Ladies' Entertainment—Mrs. Lewis J. Moorman, Chairman; Mrs. H. Dale Collins and Mrs. F. Redding Hood, Vice-Chairmen.

Book Reviews

Continued from page 705

Practical Proctology. By Louis A. Buie, A.B., M.D., F.A.C.S., Head of Section on Proctology, The Mayo Clinic; Professor of Proctology, The Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota. 512 pages, illustrated. Philadelphia: W. B. Saunders Company, 1937. Cloth $6.50 net.

Here is a book containing all the essentials to an understanding of the practice of proctology. In addition the author has injected three outstanding and extremely important ideas.

The first concerns the attitude of the physician and of the patient. Much is to be gained toward a more satisfactory examination, operation and convalescence by anticipating the patient's reactions so that he may be forewarned and reassured before they have occurred.

The second is the detailed discussion of the underlying pathology which is necessary to an intelligent interpretation of symptoms and a proper plan of treatment.

The third is a rather revolutionary attitude toward the prognosis of pruritus ani, bringing out the thought that many cures may be effected in heretofore intractable cases if sufficient diligence and perseverance are exerted to determine the etiological factor.

The Conquest of Cholera, America's Greatest Scourge. By J. S. Chambers, M.D., Professor of Hygiene and Public Health and Director of Student Health Service, University of Kentucky. 366 pages, illustrated. New York: The Macmillan Company, 1938. Cloth $4.75.

If this book can overcome the handicap of the title, its popularity will be assured; for both the subject matter and the free-flowing reportorial style will appeal to the laity as well as the physician.

This style reminds one of a good newspaper account of a current catastrophe and the great waves of this scourge which swept the country during the past century are conveyed most realistically to the reader. This is one of the chief charms of the book.

The epidemic of 1832-33 was carried along the Atlantic Seaboard, through the Black Hawk War, along Old Man River and the Interior Valley, through the Blue Grass; later the '49 gold rush carried a fresh epidemic to California.

The epidemics of 1866 and 1873 were part of the pandemic of that period. The scourge is traced from its origin in Mecca and Calcutta to the Southern ports of the United States, and then, in a detailed, systematic way Dr. Chambers follows its spread from town to town up the Mississippi River and out its tributaries to the whole Interior Valley.

Interspersed with details and statistics of the spread of the epidemic are anecdotes and specific cases which lighten the reading and sustain the interest of the reader. There are also interesting sidelights on medical opinion of an etiology and treatment from one period to the next and the gradual transition from "Miasms to Microbes."

The book is extremely interesting and the illustrations are good.

The Biology of Human Conflict: An Anatomy of Behavior Individual and Social. By Trigant Burrow, M.D., Ph.D., Scientific Director, The Lifwynn Foundation, New York City. 423 pages. New York: The Macmillan Company, 1937. Cloth $3.50.

The first part of this book discusses man's use of symbols and labels for things and objects, and calls for an altered method of inquiry into the behavior of man.

In this type of work man himself should be the instrument of observation. Burrow suggests that the principles of Freud, Adler and others are not adequate criteria of the causative factors in neurosis and insanity; further, that all factors, as pre-sexual, religious inversion, mysticism, genius and the like make a pre-conscious mode in man's behavior.

The second part is entitled "Organism Morphology." In this is found discussion of the neuroses as a racial process and the idea that man's use of alcohol and other hypnotics is due to his recognition of the physiologic motive of his trouble. That insanity is a "body-total disease as are also crime, and other similar behavior disorders," that man must adjust himself on a biological, evolutionary and behavior basis to his fellow creatures.

The third portion presents the experimental group table and makes the students themselves the material and the observers with the object of the restoration of the sovereignty of the organism as a whole. Thus bringing about coordination in man's living that cannot be achieved by psychoanalysis or any other method alone. This book is difficult to read due to the large vocabulary of the writer and to many unfamiliar terms, even though a large glossary is at the end of the book. It will be interesting to students of psychoanalysis and psychiatry to follow the future work of the author and this group.

The Collapse Therapy of Pulmonary Tuberculosis. By John Alexander, B.S., M.A., M.D., F.A.C.S., Professor of Surgery, University of Michigan, Surgeon-in-Charge, Division of Thoracic Surgery, Department of Surgery, University of Michigan Hospital. 705 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1937. Cloth $15.00.

In 1925, Alexander published a book entitled "Surgery of Pulmonary Tuberculosis," in which he made the statement that "few physicians and surgeons are as yet aware that surgery is now curing or improving approximately two-thirds of those selected cases of far advanced pulmonary tuberculosis that other methods of treatment have failed to benefit." His recent volume, "The Collapse Therapy of Pulmonary Tuberculosis," is an exhaustive presentation of those methods of surgical therapy which have proven successful in curing or improving sufferers from advanced tuberculosis, and which are being applied with greater frequency and growing success in restoring those in whom the disease has not reached an advanced stage. The author considers collapse therapy "the only important addition to the treatment of pulmonary tuberculosis since the sanitorium was introduced more than fifty years ago."

For the physician, the author has devoted much space to a discussion of the proper selection of patients for the various collapse operations; and, for the surgeon, he has discussed in minute detail and with splendid illustrations the steps of all operative procedures.

As collaborators, certain chapters have been prepared by Max Pinner, John Blair Barnwell and Kirby Smith Howlett, Jr.

Chapter 1, a comprehensive "Perspective of Collapse Therapy," is followed by a chapter on "Evolution of Surgical Therapy." This is an interesting review of the various surgical operations which have been employed in the treatment of pulmonary tuberculosis, together with brief outlines of the part played by individual surgeons in the development of certain operations. Following these are chapters on the physiologic principles and on the pathology of pulmonary collapse. An important chapter next discusses the choice of operation, and this is followed by chapters dealing with indications, contraindications, and technical procedures in performing operations for the production of collapse of the lung.

The different operations are taken up in the following order: phrenic nerve paralysis; scalinectomy and scaleniotomy; pneumothorax; closed and open intrapleural pneumolysis; oleothorax; multiple intercostal nerve paralysis; extrapleural supraperiosteal and subcostal pneumolysis; thoracoplasty; surgical drainage of pulmonary cavities; tuberculous empyema; tuberculosis of the thoracic wall.

The clarity of the text, the abundant statistical information, the excellence of the illustrations, and the complete bibliography, together with the author's preeminence in the field of thoracic surgery, make this a volume of outstanding excellence.

Southern Medical News

TUBERCULOSIS SEMINAR

The Second Annual Tuberculosis Seminar will be held at Asheville, North Carolina, July 11-16, 1938. The number who may attend will be limited to twenty and the fee will be $10.00. Special attention will be given to early diagnosis and to both surgical and medical treatment. Adequate laboratory and clinical facilities are available. Applications will be acted upon in the order of their receipt. Dr. Karl Schaffle, Wm. LeRoy Dunn Memorial Clinic, Asheville, North Carolina, is Chairman of the Seminar.

ALABAMA

Dr. Seale Harris, Sr., Birmingham, was unanimously elected President of the Medical Association of Alabama at the recent annual meeting in Mobile.

A medical center at Tuscaloosa in conjunction with the University of Alabama and the State Mental Hospital is to be constructed. The Rockefeller and Carnegie Foundations have provided $10,000,000 for this purpose.

New appointments for 1938-39 at the University of Alabama School of Medicine, Tuscaloosa, include: Professor of Anatomy—Dr. Charles Mayo Goss, now Associate Professor of Anatomy at Columbia University College of Physicians and Surgeons, New York, New York, to succeed Dr. Philip B. Armstrong, who has been elected to the Head of the Department at Syracuse School of Medicine, Syracuse, New York. Assistant Professor of Bacteriology and Pathology—Dr. Austin Louis Joyner, now Assistant in Bacteriology and Pathology at the Rockefeller Institute in Medical Research, to succeed Dr. H. K. Fidler, who has accepted an appointment for July 1st in surgery at the Royal Victoria Hospital in Montreal, Canada. Assistant Professor of Physiology and Pharmacology—Dr. Stuart Anderson Peoples, now Assistant Professor of Pharmacology at the University of Louisville School of Medicine, Louisville, Kentucky, to succeed Dr. John H. Ferguson,

Continued on page 30

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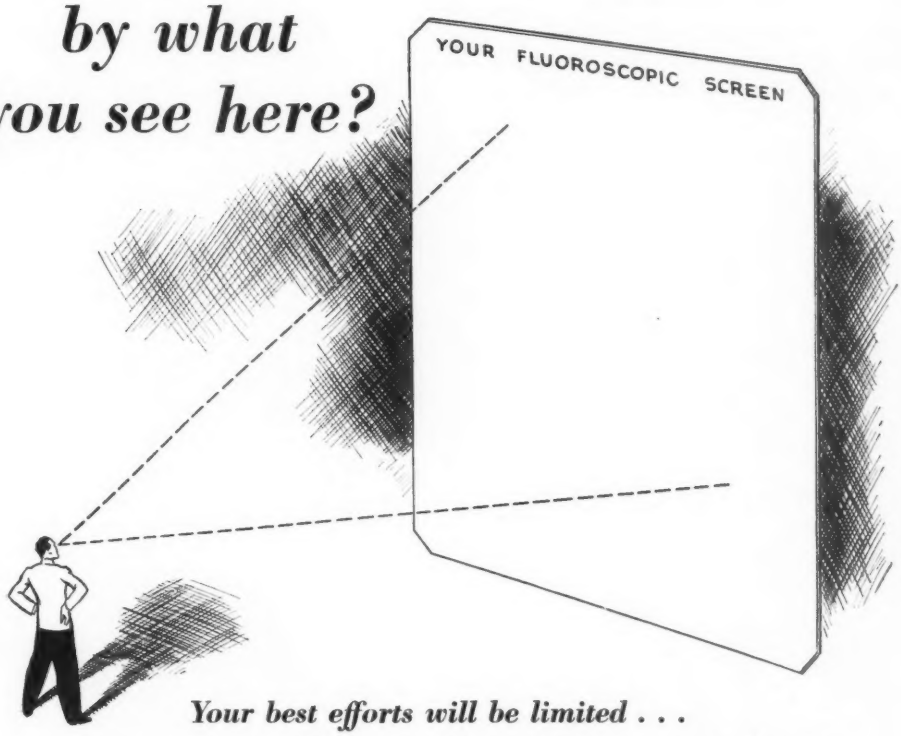

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(Either of the above courses is adaptable towards satisfying certain requirements of the various specialty boards.)

(c) Short intensive courses in special limited fields.

(d) Review courses intended for practicing physicians
(Two six weeks' courses offered each session. The first begins early January and the second mid February.)

(e) Extra-mural teaching through the Extension Division.

For detailed information write (stating type of course wanted) to

Director
Department of Graduate Medical Studies
1430 Tulane Avenue New Orleans, La.

Continued from page 708

who resigned last year to become Assistant Professor of Pharmacology at University of Michigan. Instructor in Physiological Chemistry and Medicine and Assistant on the University Student Health Service—Dr. Irl Richard Long, now Resident in surgery at St. Luke's Hospital, St. Louis, Missouri, to succeed Dr. B. M. Miller, who is going into practice at Columbia, South Carolina.

The Jefferson County Health Department sponsored an institute for Negro physicians which was held in Birmingham on March 16-17, syphilis and tuberculosis being the subjects discussed. Contributors to the program were: Dr. J. P. Robertson, Dr. Seale Harris, Jr., Dr. Clifford Lamar, Dr. Courtney W. Shropshire, Dr. W. S. Littlejohn, Dr. J. M. Townsend, Dr. Cabot Lull and Dr. L. O. Davenport, of Birmingham; Dr. J. D. Dowling, Dr. G. A. Denison and Mr. K. W. Grimley of the Jefferson County Health Department; Dr. P. W. Auston, Opelika; Dr. W. A. Maddox, Tuskegee; Dr. Kellie Joseph, Decatur; and Dr. D. G. Gill, Dr. W. H. Y. Smith, Dr. Eva F. Dodge, Dr. Holland Thompson and Dr. Charles Westover, of the State Department of Health.

Dr. Charles R. Williams, Birmingham, and Miss Alice Virginia Futral, Wadley, Georgia, were married in February.

DEATHS

Dr. Homer S. Bruce, Opelika, died recently.

Dr. Charles Edward Chapman, Mobile, aged 59, died in January of cerebral hemorrhage.

Dr. George Martin Guthrie, Inverness, aged 62, died January 9 of influenza.

Dr. John W. Fleming, Sr., Salitpa, aged 88, died recently.

Dr. John Decard Hall, Chavies, aged 69, died January 31 of carcinoma of the prostate.

Dr. Eugene Walker Hart, Dadeville, aged 74, died January 27 of chronic cardiorenal disease.

Dr. Charles Alexander Jordan, Cragford, aged 78, died February 6 of cardiorenal disease.

Dr. William Allen Mason, Uriah, aged 61, died February 19 of acute dilatation of the heart.

Dr. Etheridge Winchester Murphree, aged 73, died recently at the home of his daughter in Tarrant.

Continued on page 31

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For the reduction of edema and to diminish dyspnoea, give 1 to 3 tablets of Theocalcin, three times a day. Theocalcin, theobromine-calcium salicylate is a well-tolerated diuretic and myocardial stimulant for oral administration.

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(*See reverse side of this page*)

Continued from page 30

Dr. William Sparks McElrath, Cedar Bluff, aged 62, died February 2 of diabetes mellitus.

Dr. Marvin Simeon Stough, Dothan, aged 60, died January 3.

Dr. Isaac David Wood, Sylacauga, aged 63, died January 30 of pneumonia.

ARKANSAS

Dr. W. T. Wootton, Hot Springs National Park, has been appointed a member of the Council of the Southern Medical Association from Arkansas for the unexpired term of Dr. Harvey S. Thatcher, deceased, the appointment having been announced recently by the President, Dr. J. W. Jervey, of Greenville, South Carolina. Dr. Wootton will serve until the close of the annual meeting in 1939.

At the sixty-third annual session of the Arkansas Medical Society, held at Texarkana, April 18-20, the following officers were elected: Dr. A. S. Buchanan, Prescott, President-Elect; Dr. R. R. Kirkpatrick, Texarkana, First Vice-President; Dr. C. H. Hinkle, Batesville, Second Vice-President; Dr. S. W. Douglas, Eudora, Third Vice-President; Dr. R. J. Calcote, Little Rock, Treasurer; and Dr. W. R. Brooksher, Fort Smith, Secretary. Dr. S. J. Wolfermann, Fort Smith, was installed as President for 1938-39.

Dr. R. R. Kirkpatrick, Texarkana, was elected President of the Tri-State Eye, Ear, Nose and Throat Society in April.

Dr. R. Q. Patterson, Little Rock, was recently made a Fellow of the American Academy of Dermatology and Syphilology.

Dr. S. F. Hoge, Little Rock, has been reelected Secretary of the Arkansas Tuberculosis Association.

Dr. W. B. Grayson, Little Rock, and Dr. Euclid Smith, Hot Springs National Park, were each recently elected a Fellow of the American College of Physicians.

Dr. O. W. Hope has been elected mayor of Sheridan.

Dr. J. T. Altman has been elected President of the Jonesboro Rotary Club.

Dr. Dewell Gann, Jr., has been elected Surgeon of the Robert C. Newton Camp, Sons of Confederate Veterans, Little Rock.

Dr. L. P. Good, Texarkana, has been elected a member of the Western Surgical Association.

Dr. J. M. Walls is building a hospital at Blytheville.

Dr. Ross Fowler and Miss Jacqueline Mallioux, of Harrison, were married on March 11.

Dr. H. K. Wright, Hot Springs National Park, and Miss Lucy Adalene Davis were married on March 10.

Deaths

Dr. John A. Henry, Hope, aged 76, died January 30 of chronic nephritis.

Dr. M. C. L. Kirksey, Dardanelle, aged 68, died January 16 of hypertensive heart disease.

Dr. John Waring Lewis, Keo, aged 58, died February 9 of pneumonia following influenza.

Dr. Charles B. McLaughlin, Fordyce, aged 75, died January 28 of myocarditis.

Dr. Lindsey Gee Poe, Newark, aged 68, died January 19.

Dr. Carl Wilson Slusser, Green Forest, aged 58, died April 1.

Dr. Calvin B. Stark, Miller, aged 69, died February 25 of lobar pneumonia.

Dr. John James Stephens, Springfield, aged 72, died February 24 of bronchopneumonia.

Dr. Thomas C. Watson, Benton, aged 60, died April 7.

DISTRICT OF COLUMBIA

The following Washington physicians were honored at the meeting of the American Therapeutic Society recently held in New York City: Dr. Oscar B. Hunter, President; Dr. Joseph F. Elward and Dr. Lewis H. Taylor, Secretary and Chairman of the Council, respectively. Other officers elected were: Dr. Dan Sexton, St. Louis, Missouri, First Vice-President; Dr. Wilbur Duryee, New York, New York, Second Vice-President; Dr. Lee Rice, San Antonio, Texas, Third Vice-President; and Dr. Louis F. Bishop, New York, New York, Editor. The retiring President was Dr. Alphonse McMahon, St. Louis, Missouri.

Dr. Francis R. Hagner, Washington, has been reelected as a member of the Medical Defense Committee for a period of three years, at a recent meeting of the Executive Committee. The Medical Defense Committee consists of Dr. Luther H. Reichelderfer, Chairman, Dr. John B. Nichols, Dr. Francis R. Hagner and Dr. Coursen B. Conklin, ex-officio.

The Washington Medical and Surgical Society held its Forty-first Annual Banquet at the Mayflower Hotel on May 19. Dr. Joseph Horgan was elected President, and Dr. Beveridge Miller, Secretary. Dr. Frank E. Gibson was in charge of the general arrangements.

Dr. V. J. Darkinski, Dr. Daniel L. Finucane, Dr. John Minor, Dr. Walter K. Myers and Dr. Isaac J. Silverman, Washington, were elected Fellows of the American College of Physicians recently.

Dr. Charles R. Reynolds, Surgeon General, Major General, U. S. Army, Washington, was recently designated by President Roosevelt as President of the permanent committee of the International Congress on Military Medicine and Pharmacy, which will meet in Washington in May 1939.

Dr. Thomas Parran, Surgeon General, U. S. Public Health Service, Washington, was recently awarded a medal by Parents Magazine for outstanding service to children. The citation praised Dr. Parran's work in control of venereal diseases.

Dr. Robert A. Hare, formerly of Santa Barbara, California, has been appointed Medical Director of the Washington Sanatorium and Hospital, Tacoma Park.

Deaths

Dr. Frank Benjamin Cogswell, Washington, aged 54, died March 28.

Dr. Thomas Benton Crisp, Jr., Washington, aged 45, died March 20.

Dr. Matilda J. Gallagher, Washington, aged 75, died February 8 of myocarditis and chronic nephritis.

FLORIDA

Dr. Leigh F. Robinson, Fort Lauderdale, was elected President-Elect of the Florida Medical Association at their recent annual meeting in Miami; Dr. Arthur H. Weiland, Coral Gables, First Vice-President; Dr. Eugene G. Peek, Ocala, Second Vice-President; and Dr. J. Ralston Wells, Daytona Beach, Third Vice-President. Dr. Shaler A. Richardson, Jacksonville, was reelected Secretary and Editor of the *Journal;* and Dr. Stewart G. Thompson, Jacksonville, Managing Director. The incoming President is Dr. W. Henry Spiers, Orlando. The retiring President was Dr. Edward Jelks, of Jacksonville. The next meeting will be held in Palm Beach.

Continued on page 32

THE JEFFERSON MEDICAL COLLEGE of PHILADELPHIA

THE ONE HUNDRED AND FOURTEENTH ANNUAL SESSION BEGINS SEPTEMBER 20, 1938, AND ENDS JUNE 2, 1939.

FOUNDED 1825. A Chartered University Since 1838. Graduates number 16,313.

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Given by Dr. Fuller Albright and Associates at the Massachusetts General Hospital. August 1-13, inclusive. All day.

Part I—Inorganic salt metabolism, parathyroid disease, metabolic bone disease, metabolic aspects of nephrolithiasis, etc.

Part II—Newer aspects of endocrinology, exclusive of parathyroid disease, thyroid disease and diabetes. Fee $100 for entire course. It is possible to register for either the first or second part of the course.

Urology

Given by Dr. George Gilbert Smith and Associates at the Massachusetts General Hospital.

July 18-30, inclusive. All day.

The course is designed for physicians who have a fair knowledge of urology and will present recent advances in urology with the purpose of bringing the physician's knowledge of urological problems up-to-date. Fee $80. Women are admitted.

Apply to Assistant Dean, Courses for Graduates, Harvard Medical School, Boston, Mass.

Continued from page 31

The Sarasota County Medical Society has elected Dr. O. H. Cribbins, President, Dr. A. L. Matthews, Vice-President, and Dr. J. E. Harris, Secretary-Treasurer, all of Sarasota.

Taylor County Medical Society has elected Dr. Ralph J. Greene, Perry, President; Dr. J. L. Weeks, Perry, Vice-President; and Dr. W. J. Baker, Foley, Secretary-Treasurer.

The following were elected officers of the Victoria Hospital, Miami: Dr. Rothwell Lefholz, President; Dr. James J. Nugent, Vice-President; and Dr. A. Buist Litterer, Secretary.

Dr. James N. Patterson has been appointed as Director of Laboratories of the State Department of Health, Jacksonville, to succeed the late Dr. Paul Eaton. Dr. Patterson was Assistant Professor of Pathology, University of Cincinnati College of Medicine, Cincinnati, Ohio, having graduated at that University in 1929.

Dr. R. R. Killinger, Jacksonville, has been elected President of the Atlantic Coast Line Railroad's Association of Surgeons. Dr. L. M. Gable, of St. Petersburg, is the Vice-President.

Dr. T. F. Hahn, DeLand, has been elected to Associate Membership in the American College of Physicians.

Dr. S. G. Hollingsworth, Bradenton, has been reappointed to the Board of Medical Examiners for a term of four years, ending July 31, 1941.

Dr. Blanche A. Burgner, Sarasota, announces the removal of her offices to 226 Park Street.

Dr. Young C. Lott, Miami, announces the removal of his offices to the Olympic Building.

Dr. John T. Macdonald, Miami, is occupying new offices in the Ingraham Building.

Dr. Charles B. Mabry and Miss Alva Davis, both of Jacksonville, were married March 11.

DEATHS

Dr. C. D. Cleghorn, Miami, aged 60, died March 26.

Dr. William Henry Cox, Brooksville, aged 75, died March 4.

Dr. Davis Forster, New Smyrna, aged 68, died March 23.

Dr. Robert H. Peacock, Winter Haven, aged 79, died November 28.

Continued on page 34

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Continued from page 32

GEORGIA

Dr. William H. Myers, Savannah, was elected President-Elect of the Medical Association of Georgia at their recent annual meeting in Augusta. Dr. Grady N. Coker, Canton, is the incoming President. Dr. E. D. Shands, Atlanta, was reelected Secretary-Editor. The next meeting will be held in Atlanta.

Blue Ridge County Medical Society has elected Dr. J. M. Daves, Blue Ridge, President; Dr. E. L. Prince, Morgantown, Vice-President; and Dr. C. B. Crawford, Blue Ridge, Secretary-Treasurer.

Ben Hill County Medical Society has elected Dr. W. P. Coffee, Fitzgerald, President; Dr. W. D. Wilcox, Fitzgerald, Vice-President; and Dr. L. S. Osborne, Fitzgerald, Secretary-Treasurer.

Bartow County Medical Society has elected Dr. R. E. Adair, Cartersville, President; Dr. A. L. Horton, Cartersville, Vice-President; and Dr. J. W. Stanford, Cartersville, Secretary-Treasurer.

Bulloch-Candler-Evans Counties Medical Society has elected Dr. B. B. Jones, Metter, President, and Dr. W. E. Simmons, Metter, Secretary-Treasurer.

Crisp County Medical Society has elected Dr. A. J. Whelchel, Cordele, President; Dr. Charlie Adams, Cordele, Vice-President; and Dr. L. O. Wootten, Secretary-Treasurer.

Dooly County Medical Society has elected Dr. V. L. Harris, Pinehurst, President, and Dr. M. L. Malloy, Vienna, Secretary-Treasurer.

Elbert County Medical Society has elected Dr. A. C. Smith, President, Dr. D. N. Thompson, Vice-President, and Dr. A. S. Johnson, Secretary-Treasurer, all of Elberton.

Franklin County Medical Society has elected Dr. Stewart D. Brown, Royston, President, and Dr. B. T. Smith, Carnesville, Secretary-Treasurer.

Grady County Medical Society has elected Dr. A. B. Reynolds, President, and Dr. J. V. Rogers, Secretary-Treasurer, both of Cairo.

Hancock County Medical Society has elected Dr. Horace Darden, Sparta, President, and Dr. H. L. Earl, Clayton, Secretary-Treasurer.

Lamar County Medical Society has elected Dr. D. W. Pritchett, President; Dr. J. A. Corry, Vice-President; and Dr. S. B. Traylor, Secretary-Treasurer, all of Barnesville.

Washington University School of Medicine

Announces the following course in

OPHTHALMOLOGY

An eight months' course in Ophthalmology for those beginning the study of diseases of the eye.

Only graduates of medical schools who have completed a year of intern service will be admitted to the course.

The course will begin October 3, 1938. Fee for the course is $800.00.

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The Registrar

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Mitchell County Medical Society has elected Dr. D. P. Belcher, Pelham, President; Dr. M. W. Williams, Camilla, Vice-President; and Dr. M. M. Burns, Pelham, Secretary-Treasurer.

Monroe County Medical Society has elected Dr. W. J. Smith, Juliette, President, and Dr. G. H. Alexander, Forsyth, Secretary-Treasurer.

Rabun County Medical Society has elected Dr. J. C. Dover, President, and Dr. J. A. Green, Secretary-Treasurer, both of Clayton.

Telfair County Medical Society has elected Dr. S. T. Parkerson, McRae, President; Dr. Frank Mann, McRae, Vice-President; and Dr. Foster P. Harbin, Lumber City, Secretary-Treasurer.

Wayne County Medical Society has elected Dr. T. G. Ritch, President, and Dr. A. J. Gordon, Secretary-Treasurer, both of Jesup.

Ware County Medical Society has elected Dr. H. A. Seaman, President; Dr. L. W. Pierce, Vice-President; and Dr. Kenneth McCullough, Secretary-Treasurer, all of Waycross.

Wilcox County Medical Society has elected Dr. Homer A. Dorsey, Pitts, President; Dr. J. M. C. McAllister, Rochelle, Vice-President; and Dr. J. D. Owens, Rochelle, Secretary-Treasurer.

The Southern Psychiatric Association will hold its next annual convention in Atlanta, October 10-11.

The Grady Hospital, Atlanta, has elected on the Medical Staff

Continued on page 36

Classified Advertisements

ASSISTANCE OFFERED TO MEDICAL WRITERS. Research. Abstracts. Translations (all languages). Papers prepared from author's data. Ten years' experience with leading physicians and appointments on medical journals of highest standing. I employ no assistants; all my work is done personally and is reliable. Florence Annan Carpenter, 1801 Sixteenth St., N. W., Washington, D. C.

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Dietitians: (a) 200-bed hospital, Kentucky, salary open; (b) 55-bed hospital, Florida, salary $100, maintenance; and (c) 100-bed hospital, Alabama, salary open; Catholic preferred.

Nurses: (a) General duty nurse, 200-bed hospital, Kentucky, beginning salary $50, maintenance; (b) Scrub nurse and suture nurse, 100-bed hospital, North Carolina, salaries open; (c) Scrub nurse, 200-bed hospital, Kentucky, salary $70, complete maintenance; (d) Assistant operating room supervisor, 100 bed hospital, Florida, salary open; and (e) Night supervisors: (1) Small hospital, Alabama, must be capable to assume full charge of hospital, salary open; and (2) 100-bed hospital, Florida, salary open.

Obstetrical Supervisor: (a) 100-bed hospital, Alabama, must be Catholic, salary open.

Instructors: (a) Practical instructress, 130-bed hospital, Alabama, salary $125, complete maintenance, must be Catholic; (b) Science instructress, Catholic, must have B.S. degree; 135-bed hospital, Alabama, salary open; and (c) Instructor of practical arts of nursing and sciences, B.S. degree required, 130-bed hospital, South; salary $117, maintenance; Southerner preferred.

X-Ray-Laboratory Technician: (a) Small hospital, Alabama, salary $75, complete maintenance.

For information communicate with Southern Bureau of Medical Profession, (Miss) Oleta Milstead, Director, The Claridge Manor, Birmingham, Alabama.

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1. "Treatment of Human Pellagra with Nicotinic Acid"—Fouts, Holmes, Lepovsky and Jukes; Proc. Soc. Exp. Biol. & Med.; 37:405. (Nov.) 1937.
2. "Relation of Nicotinic Acid and Nicotinic Acid Amide to 'Canine Blacktongue' "—Elvehjem, Madden, Strong and Wooley; Jrl. Amer. Chem. Soc. 59:1767: (Sept.) 1937.
3. "Therapeutic Administration of Nicotinic Acid in Human Beings During Health and Disease"—Spies, Cooper and Blankenhorn. (Read before the Central Society for Clinical Research, Chicago—Nov., 1937—To be published).
4. "Nicotinic Acid and the Pellagra Preventing ("P-P") Vitamin"—Harris; Chem. & Ind.; 56:1134 (Dec.) 1937.
5. "Pellagra Successfully Treated with Nicotinic Acid—A Case Report"—Smith, D.T., M.D.; Ruffin, Julian M., M.D.; and Smith, Susan Cower, M.A.; Jrl. A.M.A. 109:2054: (Dec. 18) 1937.
6. "Nicotinic Acid and Vitamin B_2"—Dann, W. J.; Science; 86:616: (Dec. 31) 1937.
7. "Pellagra and Nicotinic Acid", an Editorial—Jrl. A.M.A. 110:289: (Jan. 22) 1938.
8. "Relation of Nicotinic Acid to Human Pellagra", an Editorial, Jrl. A.M.A., 109:1203:1937 (Oct. 9).
9. "The Use of Nicotinic Acid in the Treatment of Pellagra"—Spies, Cooper and Blankenhorn; Jrl. A.M.A. 110:622:1938 (Feb. 26).
10. "Advances in the Treatment of Pellagra"—Editorial, Annals of Internal Medicine 11:1760 (March) 1938.
11. "A Note on the Relationship of Porphyrinuria to Human Pellagra"—Tom Douglas Spies, Yasuo Sasaki, Ph.D., and Esther Gross, M.S., Cincinnati, Ohio; Southern Medical Journal, Vol. 31, No. 5, May, 1938, page 483.

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Continued from page 34

Dr. Thos. P. Goodwyn, President; Dr. Chas. E. Rushin, Vice-President; and Dr. C. W. Strickler, Jr., Secretary. Dr. Russell H. Oppenheimer, Dean and Professor of Medicine, Emory University School of Medicine, has been appointed Acting Superintendent of Grady Hospital, succeeding Mr. John B. Franklin, resigned.

Dr. J. H. Nicholson, formerly of Atlanta, has moved to Madison and is located in the Baldwin Building and associated with Dr. D. M. Carter.

Dr. Harris M. Branham, Brunswick, has completed fifty years in the practice of medicine.

Dr. William Benjamin Davis, College Park, and Miss Sara Astin, Palmetto, were married in February.

DEATHS

Dr. Walter P. Deakins, Wildwood, aged 71, died February 28.

A Valuable Adjunct

in Chronic Arthritis

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Clinical reports (by Wheeldon and Main, Argy, Senturia, Woldenberg, Sullivan and Hess) indicate that Sulfur Diasporal is a valuable adjunct in the treatment of Arthritis, and that clinical results are more satisfactory than with any other method of treatment.

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NON-IRRITATING
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PRODUCERS OF
FINE DIGITALIS PRODUCTS

Dr. Howard E. Ezell, Oliver, aged 60, died March 15.

Dr. John Angus Garrard, Roberta, aged 59, died March 15.

Dr. John J. Farmer, Rome, aged 76, died March 22.

Dr. William Marion Powell, Atlanta, aged 79, died March 29.

Dr. Stafford Rambo, Bluffton, aged 71, died December 25 of coronary thrombosis.

Dr. Joseph Alexander Reeves, Whitesburg, aged 73, died December 13.

Dr. Jas. Wm. Roberts, Atlanta, aged 52, died recently.

Dr. Jedd D. Walker, Hogansville, died January 7 as the result of injuries received in a fall.

Dr. William V. Russell, Dalton, aged 68, died March 10.

Dr. Jesse Edgar Wright, Macon, aged 65, died March 21.

KENTUCKY

Boyd County Medical Society has elected Dr. M. D. Garred, President; Dr. C. B. Daniels, Vice-President; Dr. J. E. Moore, Secretary; and Dr. H. S. Swope, Treasurer, all of Ashland.

Dr. James William Tankard, formerly with the Lee General Hospital at Pennington Gap, is now at Jenkins on the staff of the Jenkins Hospital.

DEATHS

Dr. Edward Barr, Owensboro, aged 61, died February 14 of tuberculosis.

Dr. Charles Mathew Gower, Trenton, aged 67, died January 2.

Dr. Thomas O. Helm, Bowling Green, aged 78, died December 17.

Dr. Virgil Ulyssus Moss, Rockfield, aged 89, died February 2 of uremia.

Dr. Abner Columbus McCulley, Morganfield, aged 60, died February 19 of cerebral hemorrhage.

Dr. William H. Nunn, Morganfield, aged 83, died December 18.

Dr. Russell Viley Rice, Louisville, aged 38, died January 2 of nephritis and uremia.

Dr. F. C. Roark, Kodak, aged 84, died in December.

Dr. G. Frank Russell, Louisville, aged 77, died January 27 of coronary occlusion and diabetes mellitus.

Dr. John Elmer Wilson, Butler, aged 72, died December 28.

Dr. William Willis Wray, Louisa, aged 67, died January 12 of uremia and carcinoma of the bladder.

Dr. John R. Wright, Louisville, aged 68, died December 19.

Dr. J. Spencer Wright, Louisville, aged 60, died January 4 of coronary occlusion.

LOUISIANA

The American College of Physicians will hold their next meeting in New Orleans next spring. Dr. John H. Musser, past President of this organization, will be General Chairman of the New Orleans session.

Beauregard Parish Medical Society has elected Dr. Thomas R. Startor, President; Dr. J. D. Frazar, Vice-President; and Dr. R. L. Love, Secretary-Treasurer, all of DeRidder.

Bossier Parish Medical Society has elected Dr. Elda S. Coyle,

Continued on page 38

"Mesco" Ointments

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Handbook of Therapy, American Medical Association, Eleventh Edition, p. 264, 1937

LITERATURE ON REQUEST

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Continued from page 36

Plain Dealing, President; Dr. R. O. Carter, Bossier City, Vice-President; and Dr. John B. Hall, Benton, Secretary-Treasurer.

Iberville Parish Medical Society has elected Dr. R. J. Spedale, Plaquemine, President; Dr. W. E. Barber, Jr., Plaquemine, Vice-President; and Dr. Frank O. Tomeny, White Castle, Secretary-Treasurer.

St. Mary Parish Medical Society has elected Dr. J. T. Prosser, Morgan City, President; Dr. F. H. Metz, Morgan City, Vice-President; and Dr. P. S. Parrino, Franklin, Secretary-Treasurer.

Vermillon Parish Medical Society has elected Dr. J. T. Abshire, Kaplan, President; Dr. A. Landry, Delcambre, Vice-President; and Dr. M. A. Young, Abbeville, Secretary-Treasurer.

Sixth District Medical Society has elected Dr. J. L. Beven, Baton Rouge, President; and Dr. H. A. Folse, Donaldsonville, Secretary-Treasurer.

The New Orleans Graduate Medical Assembly has elected Dr. John H. Musser, President; Dr. Hilliard E. Miller, First Vice-President; Dr. H. W. E. Walther, Second Vice-President; Dr. Maurice Lescale, Third Vice-President; Dr. Max M. Hattaway, Secretary; Dr. Francis E. LeJeune, Treasurer; and Dr. Emmett Irwin, Director of Clinics, all of New Orleans.

Dr. J. M. Koelle and Dr. Julius E. Isaacson, of New Orleans, were named honorary Presidents at the recent election of officers of the Lighthouse for the Blind. Dr. A. Mattes and Dr. Monte F. Meyer were appointed to the Board.

Dr. Thomas Benton Sellers, New Orleans, attended the meeting of the International Congress of Obstetricians and Gynecologists in Amsterdam and visited clinics in the principal cities while in Europe.

Dr. Robert W. Cooper will be in charge of the new radium department of the Charity Hospital, New Orleans.

Dr. J. R. Hume and Dr. Francis E. LeJeune have been reappointed to the ear, nose and throat department and Dr. W. R. Buffington to the eye department of the Eye, Ear, Nose and Throat Hospital, New Orleans.

Dr. H. W. Kostmayer was in charge of an inactive duty course of instruction for medical reserve officers of the Fourth Corps Area of the Army and Navy, held May 9-13, by the Tulane University School of Medicine, New Orleans, at the request of the United States War Department.

Dr. Marie D'Amour and Dr. James C. Rice have been appointed to the staff of the Department of Pharmacology and Experimental Therapeutics of the School of Medicine of Louisiana State University, New Orleans.

As a result of the proceeds of the 1938 Roosevelt birthday ball, a check for $5,000 was given for Charity Hospital paralysis sufferers and $1,000 for the Louisiana Society for Crippled Children.

Dr. Samuel Karlin, New Orleans, has moved to the Physicians and Surgeons Building.

Dr. Fred K. Vaughan, New Orleans, is now located in the Medical Arts Building.

Dr. Frank L. Loria, New Orleans, is now located in the Maison Blanche Building.

The newly organized New Orleans Society for Neurology and Psychiatry has elected Dr. Gilbert C. Anderson, President, and Dr. Lewis Golden, Secretary.

Dr. W. Knowlton Hall and Dr. Fred G. Brazda have been appointed instructors in the Department of Biochemistry of Louisiana State University Medical School, New Orleans.

DEATHS

Dr. Alexander Berry Childs, Eunice, aged 57, died in January of pneumonia.

Dr. Charles Arthur Wallbillich, New Orleans, aged 57, died February 10 of cerebral hemorrhage.

Dr. Wilbur W. Warner, Bogalusa, aged 68, died January 28 of coronary thrombosis.

MARYLAND

DEATHS

Dr. Thomas Rowe Price, Glyndon, aged 72, died January 16.

Dr. F. Edward Smith, Baltimore, aged 57, died in February of cardiorenal disease.

Dr. Eugene McEvers Van Ness, Baltimore, aged 69, died January 12 of carcinoma of the pancreas.

MISSISSIPPI

Delta Medical Society has elected Dr. C. W. Patterson, Rosedale, President; Dr. G. Y. Gillespie, Greenwood, President-Elect; Vice-Presidents: Bolivar County, Dr. W. W. Hall, Shelby; Humphreys County, Dr. J. W. Barkley, Belzoni; Leflore County, Dr. J. C. Adams, Greenwood; Sunflower County, Dr. U. S. Wasson, Moorhead; Washington County, Dr. R. C. Finlay, Glen Allen; and Dr. F. M. Acree, Greenville, Secretary-Treasurer.

The Grenada Clinic, Grenada, Drs. J. K. Avent, S. B. Caruthers, R. A. Clanton, F. S. Hill and J. S. Sharp, has recently moved into a new building, erected for its own use.

The Scott County Hospital, at Morton, which opened last October, is owned by Dr. J. M. Townsend and Dr. O. J. Burnham, of Morton. Dr. G. G. Townsend is Superintendent, and other physicians on the staff are: Dr. W. E. Anderson and Dr. R. B. Austin, Forest; Dr. R. B. Baugh, Polkville; Dr. L. O. Church, Pelahatchie; Dr. O. O. Austin, Harperville; Dr. J. R. Edwards, Leesburg; and Dr. K. P. Wood, Lena. The staff officers are: Dr. J. M. Townsend, President; Dr. W. E. Anderson, First Vice-President; Dr. L. O. Church, Second Vice-President; and Dr. G. G. Townsend, Secretary-Treasurer.

Dr. Felix J. Underwood, State Health Officer, Jackson, was recently elected President of the State and Provisional Health Authorities of North America at its recent annual meeting in Washington, District of Columbia.

Dr. F. M. Acree, Greenville, has associated with him Dr. Roger John Williams, formerly of Hot Springs, Arkansas.

Dr. Ira P. Burdine and Miss Mary Elizabeth Poe, of Amory, were married recently.

DEATHS

Dr. Daniel Sarter Johnson, Jr., Braxton, aged 60, died in December.

MISSOURI

The American Public Health Association will hold its next annual meeting in Kansas City, October 25-28.

The Bates County Medical Society has elected Dr. E. E. Robinson, Adrian, President, and Dr. Charles A. Lusk, Jr., Butler, Secretary and Treasurer.

Continued on page 40

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More than fifty million one ounce doses of Vita-Food Dried Brewers' Yeast have gone into the pellagra sections of the South with uniformly satisfactory results in the treatment of pellagra. Vegex has an established medical record for high pellagra preventive potency, in the Southern States, Italy and Egypt.

The Health Departments and the Red Cross have pioneered. Where the Health Department has opened the field we have cooperated, as the Health Departments have requested, to the end that people with pellagra or any other disease be gotten to the physician; and that the physician shall have an available supply, sold, as Dr. Goldberger requested, "at a price the poor can pay," which will leave something in the patient's pocketbook to help pay for the diagnoses and other needed treatment.

VEGEX

Vegex extracts the B vitamins and minerals from the grain grown yeast into more available form. The autolyzing process gives the yeast proteins a tasty meat-like flavor. The Vegex process either concentrates from the yeast or develops the extrinsic factor (anemia). There are now fifty-six reports from medical centers showing the value of Vegex in anemias; particularly in macrocytic and pernicious anemias. Physicians report Vegex a distinct aid to the liver extract treatment. Sturgis, Wills, Vaughan and others used it successfully without liver extract. We have been conservative about this; just pass the facts on to the practitioner.

Vegex was the pioneer product used in the mass treatment of beriberi during the World War; was selected to find the relation of the B vitamins to child growth; the promotion of lactation; in the pioneer studies in gastro-enterology; in disorders relating to diabetes. Being carbohydrate free, it is valuable in carbohydrate restricted diets.

Milk, for example, is low in some of the B vitamins and in iron. Vegex splendidly supplements milk for child feeding. With Vegex children generally drink more milk.

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In general use, it is now known that the B vitamin complex stimulates appetite, and aids the physician in getting a strength response from the patient. There has been much reported use in post-operative liquid diets.

Samples for clinical or physician's personal use sent on request. No sampling except when requested.

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Continued from page 38

Stoddard County Medical Society has elected Dr. Wm. J. Hux, Essex, President; Dr. S. S. Davis, Dexter, Vice-President; and Dr. Frank LaRue, Secretary-Treasurer.

The St. Louis County Medical Society and the County Health Department recently sponsored a program for conservation of eyesight. Members of the committee in charge were Dr. Clyde F. Dyer, St. Louis, Chairman; Drs. Alan D. Calhoun, Leslie C. Drews, Alonzo G. Hobbs and Clarence L. Hobbs, all of St. Louis; and Drs. William H. Bailey and Walter A. Zeitler, both of Jennings.

DEATHS

Dr. Joseph G. Beaty, Chilhowee, aged 71, died March 24.

Dr. Robert E. Crabtree, Amsterdam, aged 66, died March 14.

Dr. J. O. Ficke, Salem, aged 66, died March 22.

Dr. Enoch N. Gentry, Sturgeon, aged 83, died February 13 of arteriosclerosis.

Dr. John Roseman Marshall, Union, aged 37, died February 12 of septicemia.

Dr. James W. Mott, Poplar Bluff, aged 74, died February 19.

Dr. Henry Jacques Ravold, St. Joseph, aged 74, died in January of coronary occlusion.

Dr. John Hughes Rothwell, Liberty, aged 79, died January 6.

Dr. John H. Sampson, St. Joseph, aged 81, died February 10 of pneumonia.

Dr. John C. Scott, Lebanon, aged 66, died in January of pneumonia.

Dr. Martha J. Short Wright, Rolla, aged 76, died January 10.

Dr. Cullen Owen Thomas, Worthington, aged 59, died December 25.

Dr. Larkin E. Williams, Clever, aged 66, died January 4.

NORTH CAROLINA

Dr. William deB. MacNider, of the University of North Carolina School of Medicine, Chapel Hill, was elected recently to membership in the National Academy of Sciences.

Burke County Medical Society has elected Dr. J. B. Helms, President; Dr. J. W. Ervin, Vice-President; and Dr. Edith A. Woodwin, Secretary-Treasurer, reelected, all of Morganton.

Dr. W. H. Kibler, Morganton, spent several weeks in special study at the Medical School of Harvard University.

Dr. Ralph J. Sykes, Health Officer of Surry County, is doing some special work in venereal diseases at Johns Hopkins Medical School. Dr. Gaston W. Rogers, formerly of Raleigh, a retired officer of the Medical Corps of the United States Army, will perform the duties of Dr. Sykes during his absence of three months.

Dr. B. S. Troutman, formerly of Winston-Salem, is now associated with the Dula Hospital, Lenoir, in the general practice of medicine.

Dr. J. C. Wilkins has been declared the most useful citizen of Haw River in 1937.

Dr. John William Straughan and Miss Helen Ann Ward, both of Warsaw, were married March 24.

Dr. William T. Ward, Raleigh, and Miss Mary Powell Ward, Franklinton, were married in December.

DEATHS

Dr. Noah Bunyan Adams, Murphy, aged 69, died January 20 of arteriosclerosis and hypertension.

Dr. Ivan Proctor Battle, Rocky Mount, aged 57, died February 20 of angina pectoris due to coronary occlusion.

Dr. C. H. Bynum, Kinston, aged 65, died January 9 of cerebral hemorrhage and nephritis.

Dr. James I. Campbell, Norwood, aged 63, died January 15.

Dr. Stephen Webb Davis, Charlotte, aged 44, died March 16.

Dr. Louis Burgin McBrayer, Southern Pines, aged 68, died April 1.

Dr. John W. Wood, Boiling Springs, aged 66, died January 15 of pneumonia.

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OKLAHOMA

Dr. Harry R. Cushman, Clinton, has been appointed County Health Superintendent of Custer County.

Dr. Joseph Fulcher, Tulsa, announces the opening of his office in the Medical Arts Building.

Dr. E. K. Witcher, Tulsa, announces the opening of his office in the Medical Arts Building for the practice of internal medicine.

Dr. George A. Kilpatrick, McAlester, recently made an extensive tour of the medical centers on the Pacific Coast.

Dr. E. P. Hathaway, Lawson, has been appointed County Superintendent of Comanche County.

DEATHS

Dr. S. E. Cummings, Ravia, aged 69, died February 10 of injuries received in an automobile accident.

Dr. Oscar Vananda Guthrie, County Line, aged 51, was killed February 7 in an automobile accident.

Dr. William Luther Miller, Oklahoma City, aged 75, died January 6 of cerebral hemorrhage.

Dr. Joseph Alexander Milroy, Okmulgee, aged 67, died February 7.

Dr. George W. Wiley, Norman, aged 63, died December 31.

SOUTH CAROLINA

Ridge Medical Society has elected Dr. J. N. Crafton, Modoc, President; Dr. P. A. Brunson, Ridge Springs, First Vice-President;; Dr. A. R. Nicholson, Edgefield, Second Vice-President; Dr. A. S. Ballinger, Third Vice-President; and Dr. W. P. Timmerman, Batesburg, Secretary, reelected.

The President of the South Carolina Medical Association has appointed a committee for the purpose of gathering, preserving and publishing material which bears upon the history of the Association and of medicine generally in South Carolina. This committee consists of Dr. J. I. Waring, Charleston, Chairman; Dr. Robert Seibels, Columbia; Dr. Hillyer Rudisill, Charleston; Dr. Lin C. Shecut, Orangeburg; and Dr. Lesesne Smith, Spartanburg.

The educational campaign, sponsored by the American Society for the Control of Cancer, is progressing by the work of the Committee from the State Society, composed of Dr. J. R. Allison, Columbia, Chairman; Dr. Hugh Smith, Greenville; Dr. William Sheridan, Spartanburg; Dr. J. R. Young, Anderson; Dr. E. M. Hicks, Florence; Dr. James McLeod, Florence; Dr. K. M. Lynch Charleston; and Dr. Chas. Mobley, Orangeburg.

Dr. Douglas Jennings, Bennettsville, is Chairman of the Early

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ORETON—MALE SEX HORMONE

Extensive research by outstanding clinicians has revealed the efficacy of greater strengths of Oreton (testosterone propionate) in some of the conditions treated. Schering Corporation, therefore, introduces the 10 and 25 mgm. concentrations which should bring still further advances in male sex hormone therapy.

Steadily increasing use of Oreton and improved production technic make it possible to supply this material at half previous prices. Male hormone therapy is now within the reach of more of your patients.

Oreton is being found effective in *benign prostatic hypertrophy*, and frequently gives definite relief from such symptoms as nocturia and micturition. In the so-called *male menopause*, Oreton produces general tonic action, and relieves nervous tension, fatigue, and inability to concentrate. Diverse manifestations of *hypogonadism* in younger individuals have responded to the male hormone. Oreton has also shown encouraging results in certain cases of *impotence*.

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	Boxes of 6 amps.	10.80
	Boxes of 50 amps.	76.80
25 mgm. per 1 cc. ampule	Boxes of 3 amps.	11.15

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BLOOMFIELD, NEW JERSEY

Continued from page 40

Diagnosis Committee of the South Carolina Tuberculosis Association.

Dr. J. R. Langford, Swansea, recently celebrated his eighty-second birthday.

Dr. R. B. Durham, President of the Columbia Medical Society, has appointed a Committee on Maternal Health to study the advisability of establishing a Birth Control Clinic, the Committee consisting of Dr. W. A. Hart, Chairman, and Dr. George T. McCutcheon, both of Columbia.

Dr. E. L. Horger has been elected to the Board of Directors and Vice-Presidency of the Rotary Club of Columbia.

Dr. S. E. Miller, Martin's Point, has accepted the position of Resident Physician at the South Carolina Sanatorium, State Park.

Dr. J. Lloyd Mims, Batesburg, and Miss Virginia Maynor, Winston-Salem, were married April 9.

Dr. Andrew Burnet Whitaker and Miss Phebe Greenleaf Knight, both of Camden, were married in December.

DEATHS

Dr. Robert O'Neal Boyd, Clover, aged 32, died February 3 of pneumonia following influenza.

Dr. James L. B. Gilmore, Holly Hill, aged 79, died February 19.

Dr. Stephen Madison McCaskill, Camden, aged 66, died February 2 of chronic myelitis.

TENNESSEE

The Vanderbilt University School of Medicine, Nashville, will conduct a combined professional postgraduate course and a conference on medico-military problems for Medical Reserve Officers of the Army and Navy from June 6 to 7, inclusive.

Dr. W. E. Garrey, Professor of Physiology at Vanderbilt University School of Medicine, has been reelected President of a national federation of four allied medical-scientific societies, the American Physiological Society being the oldest of the group.

Dr. A. Stamper, Public Health authority of Belgrade, Jugoslavia, and fellow of the Rockefeller Foundation, recently visited Vanderbilt University School of Medicine to discuss international problems in medicine and public health.

Dr. M. K. Moulder, Nashville, announces the opening of his offices in the Doctors Building, practice limited to urology.

Dr. John C. Turley and Miss Katherine Matthews, both of Memphis, were married January 7.

DEATHS

Dr. Ross Anderson, Memphis, aged 30, died May 3.

Dr. Edgar Poe Blair, Nashville, aged 70, died December 12.

Dr. Jether J. Crawley, Greenfield, aged 56, died February 7 of heart disease.

Dr. H. M. Davis, Leapwood, died January 21.

Dr. Robert French Ferguson, Clarksville, died January 21.

Dr. Joshuaway Ilar Glover, Union City, aged 57, died February 14 of chronic nephritis.

Dr. Henry A. Hart, Memphis, aged 54, died February 21 of hypernephroma.

Dr. William Thomas Buck, Beech Bluff, aged 64, died December 14.

Dr. J. W. Stevens, Nashville, aged 58, died March 18.

Dr. Thomas Obadiah Senior, Nashville, aged 54, died January 8 of chronic appendicitis and cholecystitis.

For the pregnant and the nursing mother—

HORLICK'S, the Original Malted Milk, appeals to the mother whether it is prepared with water or milk. Not only is Horlick's delicious, but it affords a simple way of increasing the caloric and milk solids intake, especially desirable during the child's early development.

The increased digestibility of the milk, due to the greatly lowered curd tension resulting from the Horlick processing, is often of benefit in the nausea associated with pregnancy.

As a supplementary food when breast milk is insufficient, Horlick's is found to be practical, safe and beneficial.

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TEXAS

Six County Medical Society has elected Dr. R. B. G. Cowper, Big Spring, President; Dr. L. W. Liggett, Midland, Vice-President; and Dr. Frank B. Boyle, Big Spring, Secretary-Treasurer.

Falls County Medical Society has elected Dr. J. Walter Torbett, Jr., President; Dr. H. P. Curry, Vice-President; and Dr. Walter S. Smith, Secretary-Treasurer, all of Marlin.

The George A. Griffiths Memorial Hospital, Paris, was dedicated February 13. This two-story institution was constructed at a cost of $50,000, made possible by a grant of $25,000 and a building site provided in the will of the late Mrs. Millie Griffiths. Dr. L. P. McCuistion is chief surgeon and Medical Director; Dr. M. L. Johnson, orthopedic surgeon; and Dr. L. L. McDougal, Jr., pediatrician.

The Alpha Epsilon Delta, honorary premedic fraternity, chapter at the University of Texas, held its annual banquet recently, at which Dr. E. H. Cary, of Dallas, served as toastmaster.

A new hospital is being built at Fredericksburg by Dr. Victor Keidel which will contain thirty-one rooms.

Dr. D. C. Eiland, Munday, has been doing postgraduate work in cardiovascular diseases at the New York Postgraduate Medical School.

Dr. John C. Aarni has moved from Forney to Hayden, Arizona.

Dr. J. C. Baker has moved from Fort Worth to Azle.

Dr. W. W. Britton has moved from El Paso to New Orleans, Louisiana.

Dr. Loyd Deason has moved from Henderson to Norton, Kansas.

Dr. M. P. Knight has moved from Kermit to Iowa City, Iowa.

Dr. Willa Louise Pierce has moved from Chicago, Illinois, to Aubrey.

Dr. F. N. Shipp has moved from Port Arthur to Goodrich.

Dr. H. P. Thomas has moved from San Antonio to Waco.

Dr. F. K. Turney has moved from Robert Lee to San Angelo.

Dr. Paul L. White has moved from Dallas to Austin.

Dr. Bernie J. Wilkerson has moved from Houston to Midland.

Dr. Glenn De Vere Carlson and Miss Lorraine Frances Manske, both of Dallas, were married in December.

DEATHS

Dr. Warren Telemichus Binion, Cumby, aged 81, died March 21 of carcinoma of the larynx.

Dr. Hiram Roscoe Gilliam, Houston, aged 65, died February 11 of pyloric stenosis, duodenal ulcer and pneumonia.

Dr. L. A. Barnes, Huntsville, aged 57, died January 27 of angina pectoris.

Dr. Edgar Vernon Henry, Beaumont, aged 46, died March 19 of carcinoma of the pancreas.

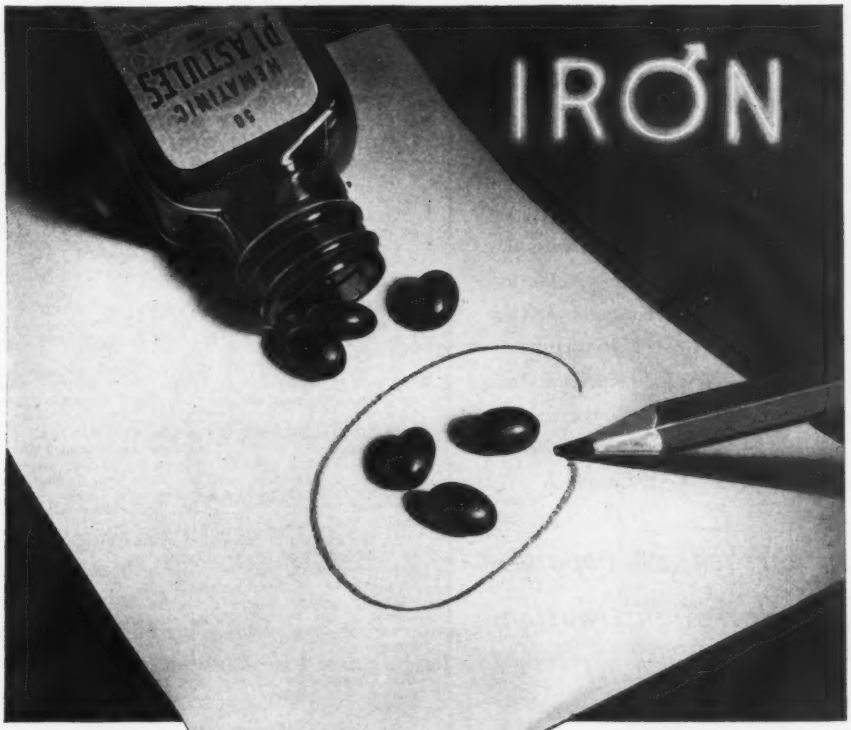
Dr. Charles DeWitt Hibbetts, Naples, aged 58, died March 1 of uremia.

Dr. Hubbard K. Hinde, San Angelo, aged 46, was killed instantly in an automobile accident March 18.

Dr. Andrew J. Marberry, San Angelo, aged 84, died January 2 of arteriosclerosis and heart disease.

Dr. Louis H. Kirk, Austin, aged 60, died March 22 of empyema and myocarditis.

Continued on page 44



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Irregular Menstruation

Bottles of 40 tablets

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Continued from page 42

Dr. Isaac B. Nofsinger, Elgin, aged 73, died February 13 of angina pectoris.

Dr. Howard Coleman Scott, Sweetwater, aged 76, died February 11 of complications following burns.

Dr. Edmund Byrd Parsons, Palestine, aged 73, died March 13.

Dr. William Thomas Thompson, Texarkana, aged 53, died January 26 of cerebral hemorrhage and hypertension.

Dr. William B. Treadwell, Lufkin, aged 81, died March 5.

Dr. John B. Winn, Hamilton, aged 82, died January 22 of mitral regurgitation.

Dr. Claude Wolcott, Amarillo, aged 66, died January 5 of angina pectoris.

VIRGINIA

The Patrick-Henry Medical Society has elected Dr. D. L. Fleshman, Bassett, President; Dr. J. T. Shelburne, Critz, Vice-President; and Dr. F. B. Teague, Martinsville, Secretary-Treasurer.

Williamsburg-James City County Medical Society has elected Dr. E. B. Kilby, Toana, President; Dr. J. R. Tucker, Williamsburg, Vice-President; and Dr. I. S. Zfass, Williamsburg, Secretary-Treasurer.

At the annual meeting of the Virginia Tuberculosis Association in Richmond Dr. Roy K. Flannagan was elected Secretary.

At the Virginia Hospital Association meeting recently, which was held in conjunction with the associations of North and South Carolina, it was decided to hold the 1939 Tri-State Conference at Old Point Comfort. Dr. J. M. Shackelford, Martinsville, was elected Vice-President.

At the meeting of the American Association for Thoracic Surgery, held recently in Atlanta, Georgia, Dr. I. A. Bigger, Richmond, was elected Treasurer; and Dr. Richard Meade, a former Virginian, now of Philadelphia, Secretary.

The Richmond Chapter of the Davidson College Alumni Association, at its annual meeting recently, elected Dr. Porter P Vinson, Richmond, President, and Dr. Richard C. Neale, Vice-President.

Dr. John O. Hurt, who has been engaged in general practice at Bent Mountain for the past year, has returned to his former position on the medical staff of the Western State Hospital at Staunton.

Dr. Linwood Farley has been reelected Chief Health Officer of Hanover County.

Dr. Francis W. Upshur, Richmond, has been appointed to direct a program for the control of venereal disease in that city, and $6,000 has been appropriated to finance the work. Dr. Upshur at one time was in charge of venereal disease wards in the U. S. Marine Hospital, Boston, and during the World War was in charge of the division of venereal disease and diseases of the skin at the Norfolk Naval Hospital.

Dr. William Y. Garrett has been appointed Health Officer of the Prince William County Health Department. Dr. E. M. Holmes, who has been directing the activities temporarily, is now giving his entire time to Fairfax County.

Dr. Harry Golston, of Roanoke, is a Passed Assistant Surgeon of the United States Public Health Service and is now stationed at Washington, D. C., on the U. S. Compensation Commission.

At the annual meeting of the Harvard Club of Virginia Dr. Thomas F. Wheeldon, Richmond, was elected President, and Dr. Lee E. Sutton, Richmond, and Dr. Hyman Cantor, Petersburg Vice-Presidents.

Dr. Richard B. Nicholls, Norfolk, and Dr. H. Aurelia Gill, Richmond, were married April 1.

Dr. Richard Campbell Manson and Miss Mary Kathryn Taylor, both of Richmond, were married April 23.

DEATHS

Dr. Edmund Henry Lewis, Gordonsville, aged 76, died February 4 of pneumonia.

Dr. Robert E. Chumbley, Radford, aged 64, died December 31 of perforated duodenal ulcer.

Dr. Peyton S. Lewis, Richmond, aged 49, died March 10.

Dr. Edward M. Parker, Emporia, aged 79, died December 16.

WEST VIRGINIA

DEATHS

Dr. Robert Augustus Hamrick, Clay, aged 68, died January 27 of coronary thrombosis.

Dr. W. W. Kerr, Volga, aged 72, died in December.

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SIX TEASPOONFULS WILL FURNISH AS MUCH CALCIUM AS IS IN THE AVERAGE DAILY DIET
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BALTIMORE, MD., U.S.A.

Each heaping teaspoonful of Emerson's C-G Alkalizer contains a substantial quantity of calcium gluconate, regarded as the most easily-assimilable form of calcium available today.

Unlike the harsh, earthy alkali compounds, C-G Alkalizer furnishes alkali salts to the blood with no damage to normal HCl of the stomach. A goodly quantity of pure sodium citrate in every dose provides *systemic* alkalinity *physiologically*. No danger of alkalosis. Digestion is aided, *not* harmed.

For a rich source of calcium and alkali for blood and tissues, turn to C-G Alkalizer—in pregnancy deficiencies and nausea, convalescence, diarrhea, common cold; la grippe and other febrile diseases; wherever acidosis strikes.

LOW COST—PALATABLE

C-G Alkalizer costs 25% to 35% less than other good alkalizers. Its snow-white granules make a zestful, effervescent drink.

EMERSON DRUG COMPANY
BALTIMORE • MARYLAND

Use Coupon for Free Full-Size Package

EMERSON DRUG CO.
Baltimore Maryland

Please send me FREE a full-size market package of Emerson's C-G Alkalizer.

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SM-6

LOOSE STOOLS IN INFANTS

require extra diapering and inconvenience the mother

Clinically loose stools are accompanied by a dehydration which, when excessive or long continued, interferes with the baby's normal gain. A long-continued depletion of water is serious, since "the fluid requirements of an infant are tremendous. A normal infant 15 pounds in weight will frequently excrete as much as one litre of urine per day. A negative water balance for more than a very short period is incompatible with life." (Brown and Tisdall)

Moreover, when the condition is superimposed by chance infection, the delicate balance may be seriously upset, since the infant's reserves have already been drawn upon, so that resistance to infection and dangerous forms of diarrhea may be too low for safety. Every physician dreads diarrhea, which Holt and McIntosh call "the commonest ailment of infants in the summer months."

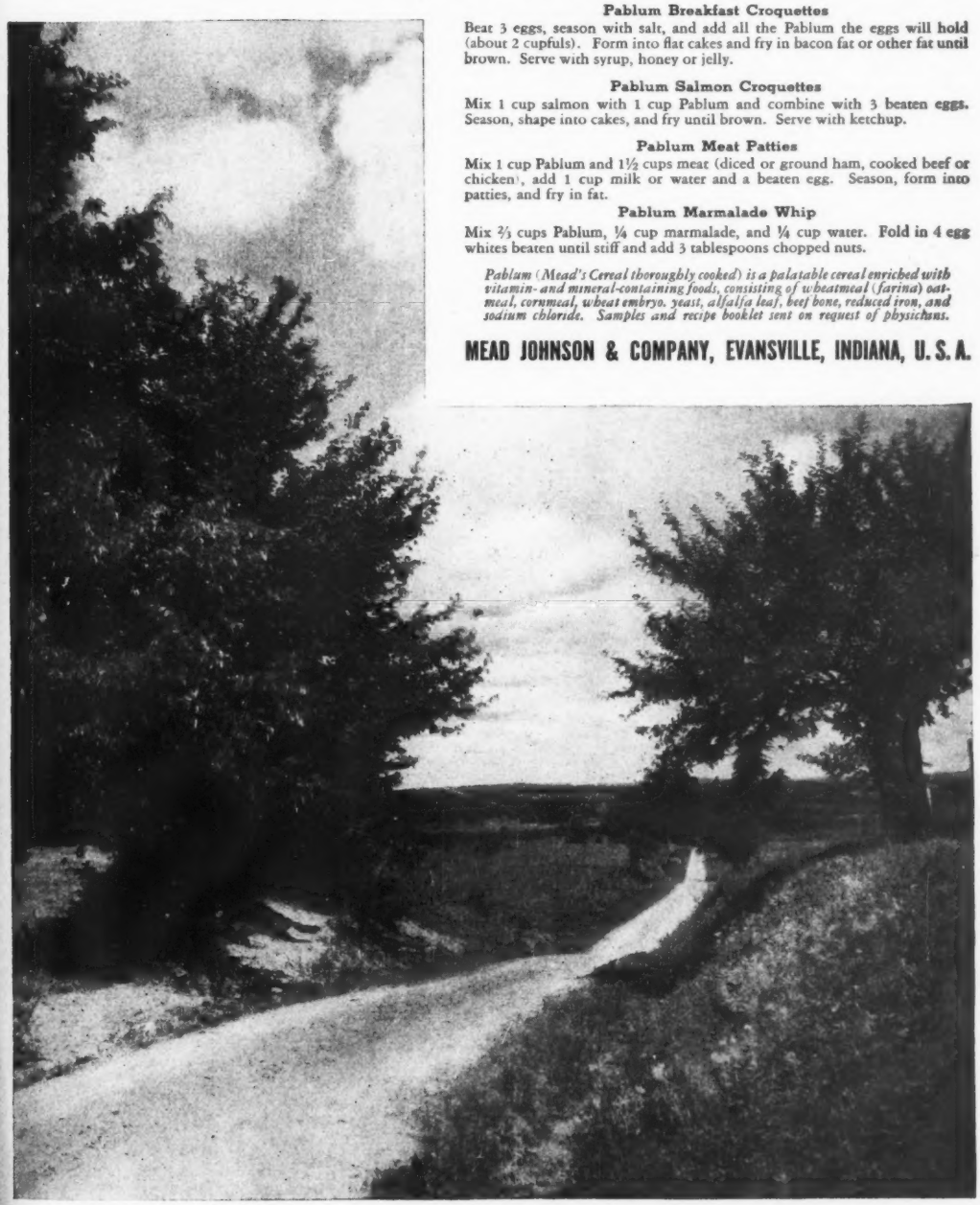
If you have a large incidence of loose stools in your pediatric practice—

Try Changing to a Dextri-Maltose Formula

MEAD JOHNSON & COMPANY, Evansville, Indiana, U.S.A.

Try PABLUM *On Your Vacation*

VACATIONS are too often a vacation from protective foods. For optimum benefits a vacation should furnish optimum nutrition as well as relaxation, yet actually this is the time when many persons go on a spree of refined carbohydrates. Pablum is a food that "goes good" on camping trips and at the same time supplies an abundance of calcium, phosphorus, iron, and vitamins B and G. It can be prepared in a minute, *without cooking*, as a breakfast dish or used as a flour to increase the mineral and vitamin values of staple recipes. Packed dry, Pablum is light to carry, requires no refrigeration. Here are some delicious, easy-to-fix Pablum dishes for vacation meals:



Pablum Breakfast Croquettes

Beat 3 eggs, season with salt, and add all the Pablum the eggs will hold (about 2 cupfuls). Form into flat cakes and fry in bacon fat or other fat until brown. Serve with syrup, honey or jelly.

Pablum Salmon Croquettes

Mix 1 cup salmon with 1 cup Pablum and combine with 3 beaten eggs. Season, shape into cakes, and fry until brown. Serve with ketchup.

Pablum Meat Patties

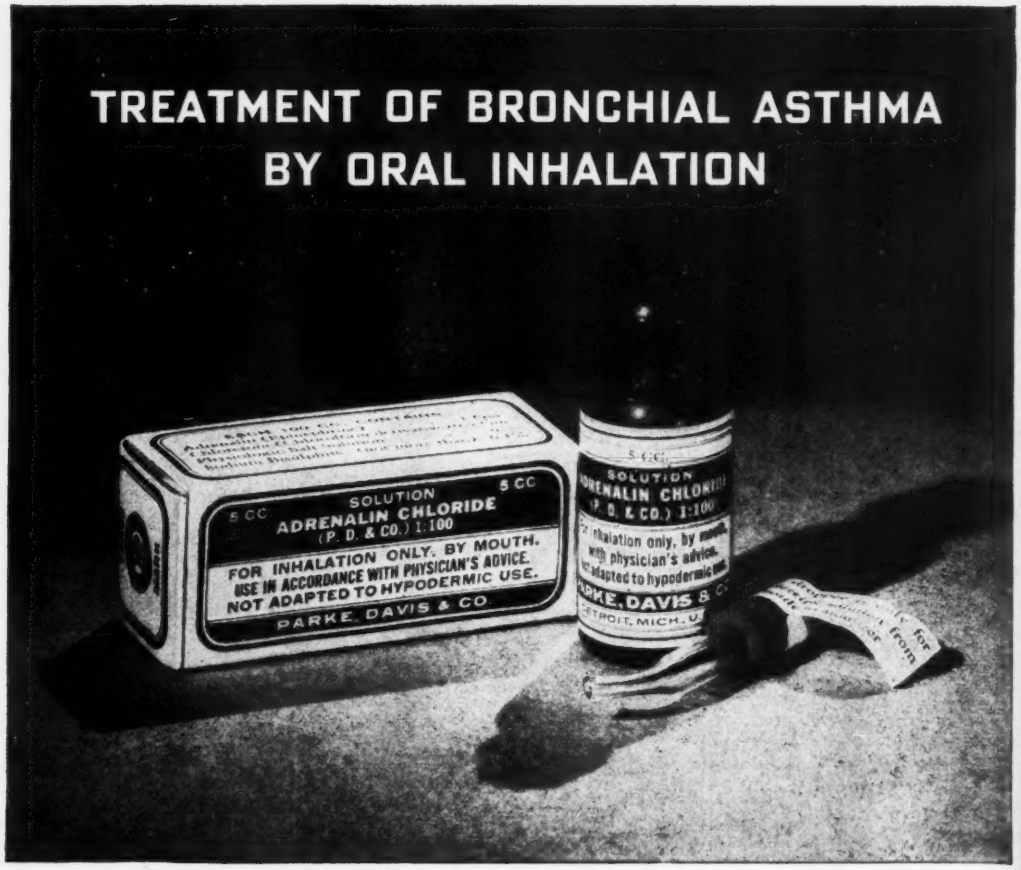
Mix 1 cup Pablum and 1½ cups meat (diced or ground ham, cooked beef or chicken), add 1 cup milk or water and a beaten egg. Season, form into patties, and fry in fat.

Pablum Marmalade Whip

Mix ⅔ cups Pablum, ¼ cup marmalade, and ¼ cup water. Fold in 4 egg whites beaten until stiff and add 3 tablespoons chopped nuts.

Pablum (Mead's Cereal thoroughly cooked) is a palatable cereal enriched with vitamin- and mineral-containing foods, consisting of wheatmeal (farina) oatmeal, cornmeal, wheat embryo, yeast, alfalfa leaf, beef bone, reduced iron, and sodium chloride. Samples and recipe booklet sent on request of physicians.

MEAD JOHNSON & COMPANY, EVANSVILLE, INDIANA, U. S. A.



ADRENALIN CHLORIDE SOLUTION 1:100

THE oral inhalation of Adrenalin Chloride Solution 1:100 is promptly effective in relieving symptoms of bronchial asthma—in most cases results have been quite as satisfactory as those following hypodermic injection of the familiar 1:1000 solution. Nervousness and tachycardia, as well as other reactions which often accompany parenteral administration, are much less frequent following inhalation therapy. Discomfort and inconvenience of hypodermic injection are obviated by this new treatment.

Adrenalin is the Parke-Davis brand of Epinephrine U.S.P. Adrenalin Chloride Solution 1:100 is accepted by the Council on Pharmacy and Chemistry of the American Medical Association; it is supplied in 5-cc. vials, together with dropper for transferring the solution to a suitable atomizer, vaporizer, or nebulizer. The apparatus used must deliver a fine spray entirely free from drops.

PARKE, DAVIS & COMPANY • DETROIT

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